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ANNALS
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AND
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LXVI

MALIGNANT MELANOMA OF THE HEAD AND NECK

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Tumors of the head and neck constitute a large portion of the practice of modern otolaryngology. The proper approach to the diagnosis and treatment of malignant melanoma of the head and neck has been a controversial subject. In recent years several interesting reports concerning malignant melanoma have been presented in the medical literature, but emphasis on this subject has been lacking in otolaryngological writings. It is the purpose of this study to survey the cases of malignant melanoma of the head and neck at the State University of Iowa Hospitals and to outline the therapy of these tumors.

Malignant melanoma imparts fear to the patient and the physician far above the actual mortality associated with them. Such terms as the "black death" and the "black cancer" immediately imply a dread, weird, and fatal disease. This is hardly the proper evaluation of this neoplasm. An extensive survey lists the five year survival rate in cases of malignant melanoma without metastases at 40 per cent and with metastases at 15 per cent, with an over all

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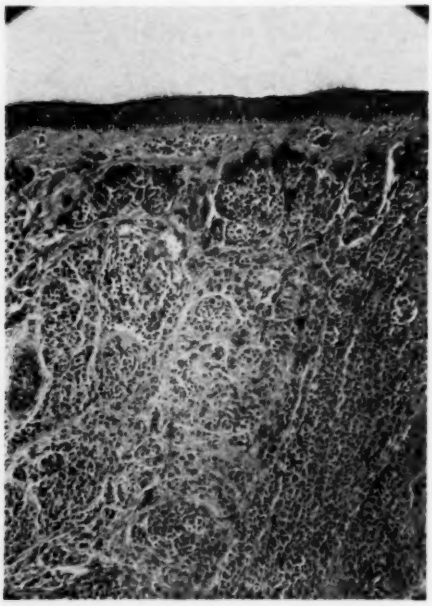

Fig. 1.—*Intradermal Nevus.* The nevus is entirely within the dermis, leaving an intermediate uninvolved zone between the epidermis and the nevus (100 x).

five year survival rate of 20 per cent.[1] In comparison, carcinomas of the lung and of the stomach have an over-all five year survival rate of less than 10 per cent.

In this report the term nevus will be used to designate lesions, pigmented or not, composed of melanoblasts[2] and not in the dermatologic sense of any congenital blemish. Every person has approximately 20 pigmented lesions scattered over the surface of the skin,[3] but the malignant melanoma has an incidence of only one in one hundred thousand[3] and constitutes only 3 to 4 per cent of all the skin cancers. This low incidence of malignant melanoma in comparison to the widespread existence of nevi makes the prophylactic removal of all pigmented lesions neither logical nor practical.

The malignant melanoma is four times more frequent in whites than in negroes,[4] and its incidence is particularly high in persons

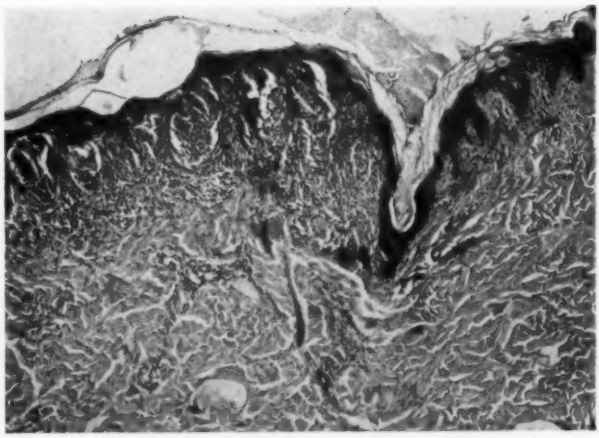

Fig. 2.—*Junctional Nevus.* The nevus is located in the basal portion of the epidermis at the junction with the dermis (100 x).

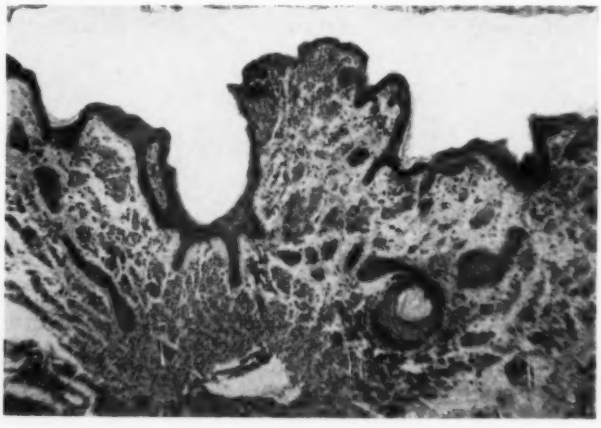

Fig. 3.—*Compound Nevus.* The nevus is composed of both dermal and junctional elements (100 x).

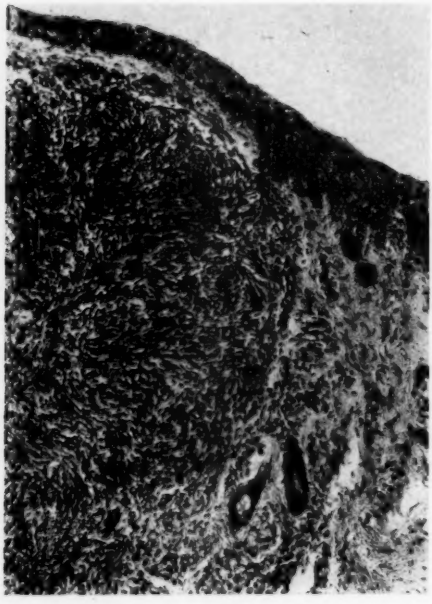

Fig. 4.—*Juvenile Melanoma.* The cellular pattern closely resembles that of a malignant melanoma; therefore, the age of the patient is essential in making the diagnosis (150 x).

with fair skin and abundant freckles. Hormonal factors influence the malignant melanoma, for its activity is frequently enhanced by pregnancy,[5] and its occurrence is rare before puberty.

There are six types of nevi. A review of these is in order to decide which nevi should be excised.

1. The *intradermal nevus* is so designated because it is located entirely in the dermis (Fig. 1). The nevus cells form masses without any encapsulation and often penetrate into the underlying subcutaneous fat. This is the commonest type of pigmented lesion, and most of the common moles belong to this group. This lesion appears as a smooth and flat, or papillary warty mole whose color ranges from light to dark brown. The hairy mole is almost always of the intradermal type. This intradermal nevus is the most stable nevus and does not undergo malignant changes. It is more common in adults

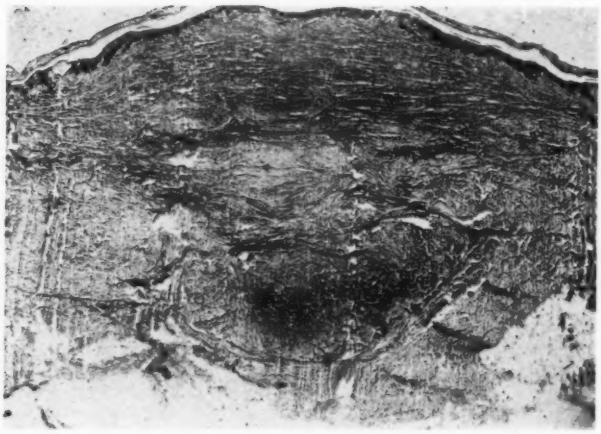

Fig. 5.—*Blue Nevus.* Note the pigmented nevus cells located deeply within the dermis (35 x).

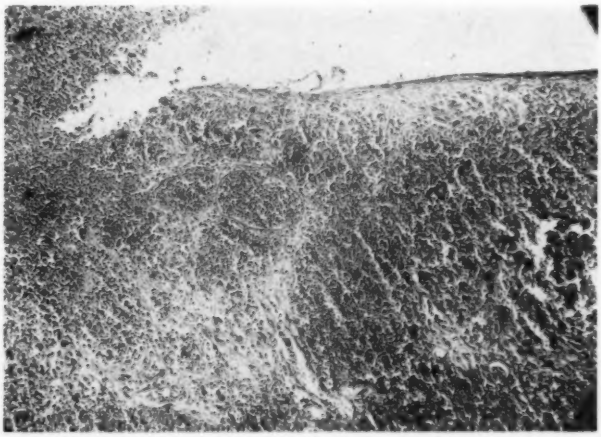

Fig. 6. — *Malignant Melanoma.* The malignant melanoma extends throughout the tissue section with only a portion of the epidermis remaining. Note the ulceration (150 x).

Fig. 7.—A malignant melanoma on the cheek of a 69 year old white female. Note the satellite foci.

and does not appear in the palm of the hand, the sole of the foot, or the genitalia.

2. The *junctional nevus* is so named because the nevus cells are located within the basal layer of the epidermis at the junction with the dermis (Fig. 2). Nevus cells are often found at the periphery of the main lesion separated by areas of normal epithelium. This arrangement explains the frequent recurrence of this type of lesion when an apparently complete surgical excision was accomplished. Clinically, the lesion appears as a pigmented nevus of brownish color. It is smooth, flat, and hairless, and it occurs mainly on the sole, palm, genitalia, and head.

Those nevi on the palm of the hand, the sole of the foot, and the genitalia are almost always junctional in type. The administration of ACTH has been reported to have initiated the appearance of junctional nevi in adults.[6] Nine out of ten malignant melanomas

arise from junctional nevi.[7] Less often, a malignant melanoma arises from a compound nevus and rarely from a blue nevus.[7]

3. The *compound nevus* is made of two elements: junctional and dermal (Fig. 3). On clinical examination this type of nevus cannot be distinguished from the previous types.[5] The junctional component occurs in 98 per cent of the intradermal nevi in children and in only 12 per cent in adults.[7] It is the junctional element which renders this nevus potentially dangerous. The activity of the junctional element in a hairy compound nevus is frequently manifested by the loss of hair.

4. The *juvenile melanomas* are usually hairless and warty, showing similar histological features to those of the malignant melanoma

TABLE I

AGE INCIDENCE

2nd Decade	2	5%
3rd Decade	1	3%
4th Decade	2	5%
5th Decade	5	14%
6th Decade	4	11%
7th Decade	10	27%
8th Decade	9	24%
9th Decade	4	11%
	37	100%

(Fig. 4) although experienced pathologists can most often distinguish between these two types.[7] It is well known that a pigmented skin lesion occurring before puberty may have histological features which resemble those of a malignant melanoma and yet pursue a benign clinical course. In our series of 37 cases no malignant melanoma was found before puberty (Table I). The juvenile melanomas have been described by Spitz,[8] and their recognition has led to the adoption of conservative surgery in the pre-puberty patient. Allen[7] has indicated that in the past the incorrect diagnosis of a juvenile melanoma as a malignant melanoma has resulted in disproportionately radical surgery and false cure rates. Juvenile melanoma occurs most frequently on the face, but the trunk and limbs may also be involved.

The removal of the juvenile melanoma is indicated for cosmetic reasons and as a prophylactic measure.

5. The *blue nevus* derives its name from the marked pigmentation which produces the characteristic color. The main cellular element is a spindle cell arranged in whorls or fascicles suggestive of a neurogenic origin. This lesion is always located in the dermis (Fig. 5). Frequent sites of occurrence are the face, the dorsum of the hands and feet, and the buttocks. Its malignant variety is extremely rare.

6. The *malignant melanomas* occur primarily on the skin and mucous membranes; those in the eye form a separate entity. The

TABLE II

LOCATION OF PRIMARY LESION

Cheek	9	24%
Scalp	7	19%
Skin of Neck	5	13%
Pre-auricular	5	13%
Eyelid	3	8%
Post-auricular	2	5%
Nose	1	3%
Ear Canal	1	3%
Auricle	1	3%
Soft Palate	1	3%
Temple	1	3%
Forehead	1	3%
	37	100%

common sites of occurrence on the mucous membrane are: nose, mouth, anorectal junction, urethra, and occasionally the larynx, bronchus, and esophagus.[2] It should be noted that a frequent location of this tumor is the head and neck area[7] which is the realm of the otolaryngologist. In the present series of cases, the cheek was the commonest site of malignant melanoma of the head and neck (Table II).

Clinically, the lesion has a warty appearance with a macular edge. Occasionally the malignant melanoma is so insignificant that its

removal may be entirely forgotten by the patient until a metastasis develops.

The following aids are stressed in the clinical diagnosis of malignant melanoma:[9]

1. Increase in pigmentation in a pre-existing mole.

2. Radical extension of a peripheral halo of pigmentation (Fig. 7).

3. Increase in size of a mole, either above the surface or radially.

4. Ulceration of a pre-existing mole (Fig. 6).

5. Presence of a metastatic pigmented lesion.

6. Location of a mole on sole of foot, palm of hand, or genitalia.

7. Hemorrhage or serous exudation from a mole.

In spite of long clinical experience with this type of tumor, an erroneous diagnosis of malignant melanoma is made in close to 50 per cent of cases of pigmented skin lesions.[10] Two conclusions can be drawn from the above statement:

1. Routine histological examination of all excised pigmented lesions should be carried out regardless of the benign clinical appearance. Omission of this study is a frequent cause of inadequate treatment.[11]

2. Radical surgery should not be performed in a patient with a pigmented lesion until histological proof of malignancy is obtained, regardless of the clinical certainly of malignant melanoma.

TREATMENT OF MALIGNANT MELANOMAS

Wide local excision with prophylactic or curative en bloc radical neck dissection is the treatment of choice in malignant melanoma of the head and neck. A review of our series shows that the initial therapy was frequently deficient (Table III).

From these figures (Table III) it is evident that when there was adequate wide excision of the malignant melanoma, a primary closure was not often possible, and in 50 per cent of the cases, skin grafting was required. It is generally agreed that a good rule to follow is to excise as much healthy skin as that grossly involved by the tumor. If this rule is followed, few primary closures can be accomplished.

TABLE III

MODE OF THERAPY

GROUP I (Patients initially treated elsewhere)			19	51%
1. Local excision by				
a) Surgery	9	25%		
b) Electrocoagulation	3	8%		
2. Local excision and skin graft	0	0		
3. Local excision and neck dissection	0	0		
4. X-ray therapy	2	5%		
5. Combined x-ray therapy and local excision	2	5%		
6. Combined x-ray therapy and electrocoagulation	1	3%		
7. Biopsy	2	5%		
GROUP II (Patients initially treated at SUI)			18	49%
1. Local excision by				
a) Surgery	6	16%		
b) Electrocoagulation	1	3%		
2. Local excision and skin graft	6	16%		
3. Local excision and radical neck dissection	1	3%		
4. Local excision, skin graft and radical neck dissection	3	8%		
5. Parotidectomy and neck dissection	1	3%		
6. X-ray therapy	0	0		
			37	100%

The time lapse between diagnosis and treatment is of extreme importance in the therapy of malignant melanoma. In this series an average of nineteen months lapsed before we were consulted in patients treated elsewhere for malignant melanoma.

When treating a patient with malignant melanoma, we prefer to perform a wide excision of the primary site followed by a prophylactic or curative radical neck dissection within a few days, for the histologic diagnosis by frozen section is not always reliable, especially in cases of questionable junctional activity and pigmented basal cell tumors. A prophylactic neck dissection is advocated in this type of lesion because of the high incidence of regional metastasis in patients in which regional node dissection was not performed,[5] and because of the high virulence of this tumor which has been compared to a Grade IV epidermoid carcinoma.[7] The excision of the intervening skin between the primary lesion and the regional metastases has been

TABLE IV

SURVIVAL RATE

INDETERMINATE CASES				17	45%
Death from other causes			2	5%	
Death cause unknown			2	5%	
No follow up			2	5%	
Inoperable when initially seen			7	19%	
Refused therapy			1	3%	
Palliative therapy			3	8%	
DETERMINATE CASES				20	55%
Death due to malignant melanoma			7	19%	
Alive and well			13	36%	
1 year	5	14%			
2 years	3	8%			
8 years	3	8%			
13 years	1	3%			
16 years	1	3%			
				37	100%

recommended by Pack,[12] and where it has been feasible, we have followed this plan.

As previously stated, there is no correlation between the pessimistic outlook maintained by some members of the medical profession and the actual mortality of malignant melanoma of the head and neck, particularly when the patients are seen early and treated adequately (Table IV).

Although surgery is the treatment of choice, the use of radiotherapy in the management of malignant melanoma has on occasion successfully controlled the tumor.[13,14] Recently the administration of triethylenephosphoramide (TEPA) has been reported[15] to have caused the regression of malignant melanoma in patients with widespread metastases.

CONCLUSIONS

A malignant melanoma can metastasize by both lymphatic and vascular channels. Occasionally there will be a case in which the

patient will have what is thought to be adequate surgical treatment (wide local excision with en bloc lymph node dissection) of a malignant melanoma of the head and neck, only to have distant vascular metastases within the lungs, liver, and brain become evident months later. Such a case is often referred to as reason against definitive surgical therapy of a malignant melanoma. However, this example is not the rule and, initially, one cannot predict which malignant melanoma is going to metastasize via the lymphatics and which will metastasize via the blood stream. Therefore, all malignant melanomas demand an aggressive surgical approach.

One cannot over-emphasize the importance of prophylaxis in the consideration of malignant melanoma. A malignant melanoma does not just suddenly appear. The great majority arise from junctional nevi which have been present for some time. The otolaryngologist must be alert and practice prophylactic excision of these junctional nevi, particularly those of the cheek which are subject to the daily trauma of the razor.

Histochemical, hormonal, and enzymatic studies most probably will play a more important role in the therapy of malignant melanoma in years to come. Presently, vigilance, expediency, and thorough initial surgery are the most important factors.

SUMMARY

1. The over-all five year survival rate of malignant melanoma is better than that of carcinoma of the stomach or lung.

2. The six main types of nevi are: 1) the intradermal nevus, 2) the junctional nevus, 3) the compound nevus, 4) the blue nevus, 5) the juvenile melanoma and 6) the malignant melanoma.

3. The malignant melanoma occurs primarily on the skin and mucous membranes (those in the eye form a separate entity). The malignant melanoma most often arises from a pre-existent junctional nevus. Junctional nevi of the head and neck are prone to become malignant melanomas and should be excised.

4. Malignant melanoma is very rare before puberty. Hormonal and racial factors influence the malignant melanoma.

5. All pigmented lesions showing activity, as evidenced by increase in size, change in color, itching, bleeding, ulceration, or crusting, must be looked upon as potential malignant melanomas.

6. Wide local excision with prophylactic en bloc radical neck dissection is the treatment of choice in malignant melanoma of the head and neck.

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LXVII

THE PRINCIPLES OF VASCULAR SURGERY IN OPERATIONS ON THE HEAD AND NECK

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For those surgeons performing major surgery of the head and neck, the basic principles of general vascular surgery assume an important facet of their armamentarium. A technique of arteriorrhaphy and vessel grafts as applied in the field of head and neck surgery including some original experimental work in vessel replacement will be described.

VESSEL INJURIES

Injuries of the major vessels in the head and neck constitute a surgical emergency. Immediate control of hemorrhage sometimes may be achieved by digital compression of the common carotid artery against the carotid tubercle of the transverse process of the VI cervical vertebra. If this emergency measure does not suffice, packing and local compression is necessary until definitive treatment can be instituted. Blind clamping is to be condemned. Airway patency must be carefully maintained and tracheostomy should be performed freely especially with any major injury near the air passages. Hematoma as well as overenthusiastic packing may cause serious compression and edema of the larynx. When this is a possibility, tracheostomy is best performed as an elective rather than an emergency procedure. Postoperative thyroidectomy hemorrhage of any magnitude usually requires tracheostomy. Compression over the carotid body is likewise to be avoided as this may produce syncope and add to the clinical picture of shock. Shock from blood loss is best treated with whole blood, plasma, or one of the plasma expanders such as polyvinyl pyrrolidone, dextran, or oxypolygelatine. Adequate

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From Department of Surgery and Surgical Research, St. Clare's Hospital, New York, New York.

Presented at the Sixth International Congress of Otolaryngology, Washington, D.C., May, 1957.

cranial blood pressure must be maintained. Narcotics are to be avoided but if absolutely necessary should be given intravenously in small doses.

The definitive care of these vascular wounds is done in the operating room. They are usually best performed under general endotracheal anesthesia or anesthesia through a tracheostomy tube.

Injury to all vessels in the head and neck except the common carotid and internal carotid arteries are treated by ligation and usually division of the vessel. The subclavian artery may be another exception to this rule when the collateral pathways are severely injured. Otherwise, the subclavian artery may likewise be ligated and divided. A partially divided vessel cannot constrict; hence, it should be ligated and then completely divided. Ligation consist of a distal suture ligature of 4-0 silk and a proximal tie of 3-0 or 2-0 silk. Adequate exposure of the wound is of paramount importance. Any blind clamping must be avoided because of the multiplicity of the important structures in the region. For example, damage to the superior laryngeal nerve or the hypoglossal nerve is a grave possibility with ligation of the external carotid artery. The same is true of facial injuries which involve the internal or external maxillary artery where blind clamping may damage a branch of the facial nerve.

Injuries of the common carotid and internal carotid arteries are best handled under the principle of re-establishing continuity. Ligation of the internal carotid artery is always hazardous while ligation of the common carotid artery may be risked if the external-internal carotid continuity is patent.

If these vessels are severely contused and if there is evidence of intraluminary clot and spasm, the clots should be carefully removed. If the walls of these vessels are severely damaged, it is best to resect the injured segment.

The basic principle of all surgical procedures on blood vessels is that of extreme care of the vessel wall. All arteriorrhaphy procedures must utilize fine suture materials such as 6-0 silk on an atraumatic needle. Extreme care to the intima is a necessity and exact approximation must be achieved. The type stitch that is used is actually of little consequence except that the edges of the repair or graft must evert; i.e., intima must approximate intima. Only a single suture layer is used consisting of sutures through and through all layers of the vessel wall. The technique may be either interrupted, everting

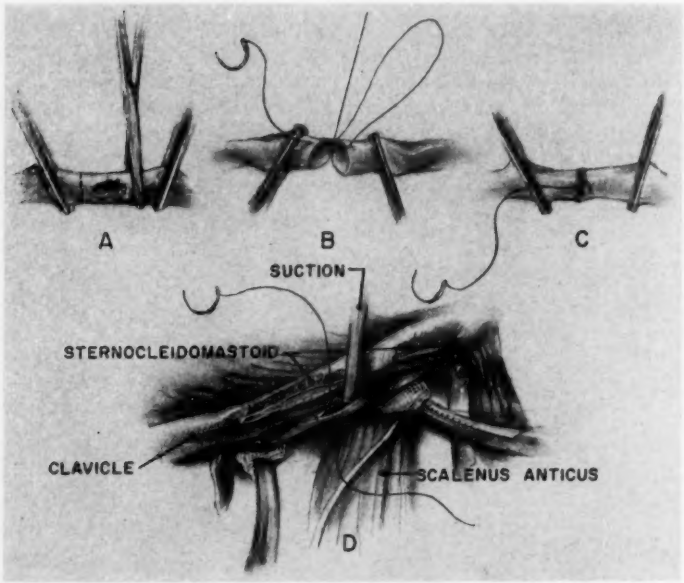

Fig. 1.—A, B, C—End to end arteriorrhaphy with excision (A) of damage segment of artery. Note (B) how the clamps rotate the vessel facilitating the placement of the posterior row of sutures.

D—Lateral venorrhaphy—Injury to the subclavian vein may be repaired in this fashion using interrupted sutures. Control of hemorrhage is achieved by gauze pressure proximally and distally against the clavicle.

mattress sutures, or simple everting continuous suture. All knots are tied on the outside of the vessel wall. The use of an anticoagulant is controversial. Heparin if so desired may be injected into the repair site during closure (100 milligrams of heparin diluted in 10 cc of normal saline solution).

During the arteriorrhaphy each end of the damaged vessel is occluded with a small bulldog type of serrefine clamp of the Pott's variety. The clamps are placed well back of the suture site. The sutures must not enter the vessel wall at the site of the clamp since the holding power of the vessel wall is impaired by the clamp. There should not be any constriction at any arteriorrhaphy site since such constriction may contribute to the so-called poststenotic dilatation of a vessel or graft. This is thought to be due to the action of hydraulic forces of the blood.

Lateral arteriorrhaphy may manage vertical lacerations only insofar as no significant narrowing of the repaired segment occurs. It is best to close such injuries horizontally if not too extensive. It is noteworthy to mention that although most venous injuries in the neck are treated by division and ligation an exception may be the subclavian vein. Injuries to this vessel may occur from accidental trauma or during a surgical procedure. If it is feasible, lateral venorrhaphy is the treatment of choice mainly because of the inaccessibiliy of the vessel as its lies immediately beneath the clavicle (Fig. 1D). The open distal end of all the great veins must be immediately compressed to prevent air embolism.

With complete division or nearly complete division, end to end arteriorrhaphy (Fig. 1A,B,C) is done by first excising any frayed or irregular portion of the vessel. Any section with damaged intima which causes intravascular clotting must be excised. The Pott's clamps on the proximal and distal ends of the vessel may be used to rotate the vessel so that one continuous posterior suture is first placed and then followed by one continuous anterior suture as the clamp is rotated back to its first position. The clamp on the distal segment is removed first so that any back bleeding may demonstrate leaks. Simple through and through sutures are placed in such bleeding sites. Not too much time should elapse before the clamp on the proximal segment is removed since delay may promote clotting at the arteriorrhaphy site. Such bleeding sites usually close with light digital pressure. Gelfoam gauze may also be used for small bleeding sites but should never be relied upon for large leaks.

When the injured segment is of such a size that simple end to end repair is impossible because of too much tension, continuity is achieved by the use of a vascular graft.

Grafts may be either autogenous, homologous, synthetic, or heterogeneous. The latter type is used only in experimental vascular surgery.

Autogenous grafts are by far the best since there is no tissue resistance and no vessel bank is necessary. They are usually venous in nature. Experimentally in our surgical research laboratories the abdominal aorta in five dogs was replaced by autogenous sections of peritoneum with varying layers of the abdominal wall for support. One dog died postoperatively from hemorrhage, the arteriorrhaphy sutures having been placed at the site of the clamps. Of the four survivors, three had patent grafts at the end of 18, 19½, and 33½

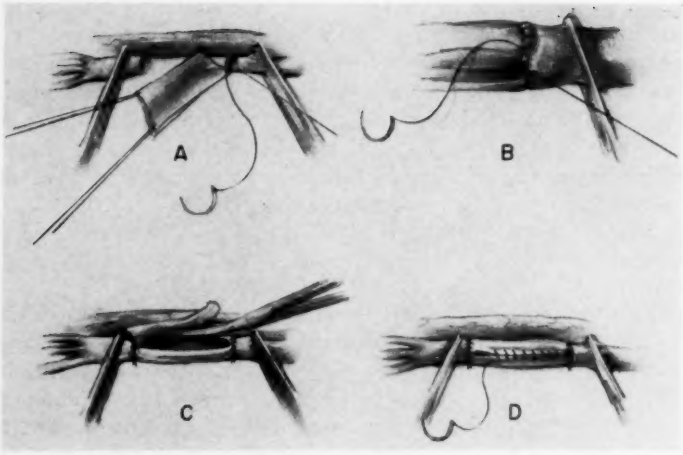

Fig. 2.—Technique of free peritoneal graft in the experimental animal. A. Rectangular section of graft is placed in vessel defect with peritoneal surface facing inward. B. A continuous suture is used for approximation at each end of the graft. C. The excess of the graft is excised. D. A continuous suture is used to close the longitudinal defect thus completing the vessel reconstruction.

months. The fourth dog had occlusion of the grafted segment, the diameter of the grafted segment being less than 5 mm in diameter, a size much too small for this type of reconstruction. This experimental technique has the advantage of freely available autogenous material. The peritoneum is of the same embryonic origin as vessels; namely, mesoderm. This discourages clot formation. The varying layers of the abdominal wall lend support to the peritoneum (Fig. 2).

Homologous arterial grafts require preservation either in 70 per cent alcohol, in formalin, in nutrient materials; e.g., Tyrode's solution, or by freeze-drying and lyophilization. If sterility is questionable, such may be achieved by radiation. As the storage time of these grafts increases, the media of the graft loses its elastic support and danger of rupture is more imminent. A limit of some five to six weeks' storage time is used by some as a rule of the thumb.

Synthetic materials either in the form of a cloth or tube are available in varying sizes. Nylon, vinyon, dacron, orlon have all

been used with varying degrees of success. The advantage of these grafts is that there is no storage problem. They may be simply sterilized by boiling. The big disadvantage lies in the tendency toward clot formation especially in the smaller lumen vessels as one would encounter in the carotid arteries.

In head and neck surgery, autogenous vein grafts are to be preferred. If either the internal or external jugular veins are available, they may be used if proper in size. Too large a diameter may tend toward aneurysmal dilatation. The long saphenous vein is ideally suited and readily available (Fig. 3). The valves in veins make it necessary to place the graft in the proper direction of flow. The length of the graft is determined in situ since the removed vein will contract and shorten. The suture technique is identical to the end to end arteriorrhaphy previously described. Heparin again is a matter of choice.

ANEURYSMS AND ARTERIOVENOUS FISTULAE

Closely allied with vessel injuries are aneurysms and arteriovenous fistulae since they are usually the late sequelae of such injuries, and the technique of their care is similar to acute vessel injuries.

Aneurysms may be true or false. True contain all the walls of the parent vessel while false ones are lined by the organized wall of the hematoma resulting from an injury or infection. True aneurysms may be either fusiform or saccular. The treatment of such aneurysms of the common carotid and internal carotid arteries consists of careful dissection with early isolation of the proximal segments so that adequate control of inadvertent hemorrhage may be achieved. The diseased segment is excised, and if end to end arteriorrhaphy is not possible, a suitable vessel graft is inserted.

Aneurysms of the subclavian artery in addition to being the result of trauma may be the result of compression by a cervical rib or associated with a scalenus anticus syndrome. This pathology exemplifies the phenomenon of poststenotic dilatation. The usual treatment is section of the scalenus anticus muscle. Another treatment of aneurysms has been described such as wrapping the aneurysm with polythene impregnated with dicetyl phosphate. This method has little application in the field of head and neck surgery. Aneurysms of any other vessels in the head and neck may be treated by proximal and distal ligation with removal of the diseased segment.

Arteriovenous fistulae, abnormal direct communication between an artery and a vein, are usually the result of trauma, less commonly

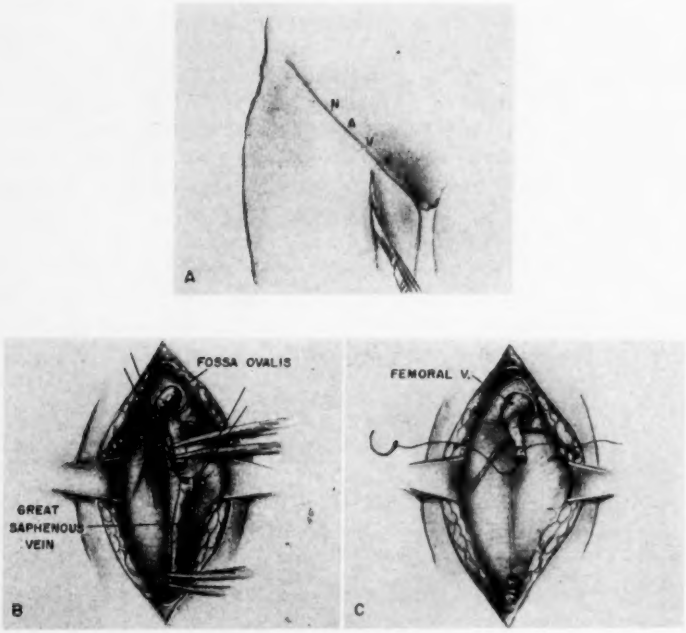

Fig. 3.—Autogenous saphenous vein graft.

A—Vertical incision placed about 2 inches below the inguinal ligament just medial to the pulsations of the femoral artery. N: Femoral nerve; A: Femoral artery; V: Femoral vein; E: Empty space (femoral canal); L: Lacunar ligament.

B—The greater saphenous vein lies superficial to the deep fascia and muscle bundles. At this level the femoral vein overlies the femoral artery.

C—The femoral vein must not be injured. The vessel ends are occluded with a proximal tie and a distal suture ligature.

on a congenital basis. When they occur in the head and neck, the site of predilection may be in the area of proximity of the common carotid artery and the internal jugular vein. Thrill and bruit are present and the patient may complain of tinnitus. Depending on the size of the communication, duration of existence, and nearness to the heart, other signs will be noted. These consist of heart failure, increased blood volume and tachycardia. Rarely bacterial endarteritis of the fistula occurs.

With digital compression over the fistula, a slowing of the pulse occurs, the Nicolodoni-Branham sign. Such fistulae rarely close

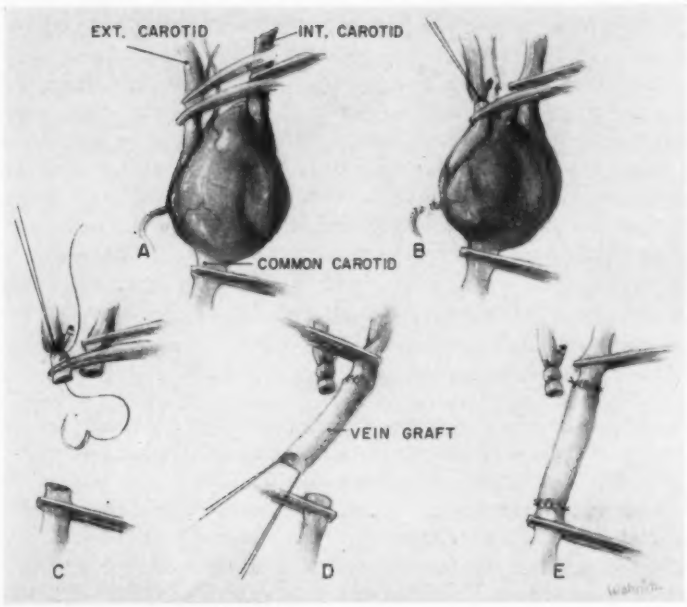

Fig. 4.—Excision of an aneurym or a carotid body tumor which involves the vessel walls at the bifurcation of the common carotid artery.

A—Isolation of all vessels and cross clamping of the carotids. Vascular clamps are used on the common and internal carotids while ordinary curved clamps occlude the external carotid artery. The time of total occlusion of the internal carotid artery blood flow must be minimal; hence, the surgery must be so planned that the graft be applied immediately following occlusion. The arteriorrhaphy may be performed before the aneurysm or tumor is removed. During the period of occlusion, cerebral blood flow must be facilitated by careful maintenance of blood pressure and blood volume. The tolerated time of occlusion is variable but should not exceed 10 to 15 minutes. If the lesion is proximal to the bifurcation more time is allowable since backflow through the external carotid artery to the internal carotid artery is possible.

B—The superior thyroid, the occipital and ascending pharyngeal arteries are ligated and transected. One clamp on the external carotid artery may be replaced by a ligature if so desired.

C—The aneurysm or tumor with the bifurcation is excised. A suture ligature is placed on the external carotid artery distal to the tie. This latter step is best deferred until after the graft is in place.

D—A vessel graft is interposed if end to end arteriorrhaphy is not feasible.

E—The completed reconstruction. Remove the distal clamp first to demonstrate any leaks at the suture sites.

spontaneously and should be treated surgically. It is only in the head and neck that a proximal arterial ligation is performed for the treatment of an arteriovenous fistula. This is only in the case of an internal carotid artery cavernous sinus fistula since there are no branches between the site of ligation and the site of the fistula. Here the internal carotid artery is totally occluded in the neck, usually along with the concomitant vein. All other fistulae require division or excision of the fistulate and re-establishment of the continuity of the artery if the latter is a vital vessel. This may be done by either dividing the fistula and performing a lateral arteriorrhaphy or by excising the fistula with the affected artery and vein and re-establishing continuity of the artery by end to end suture or interposition of a graft. Simple ligation of the fistulous tract is wholly inadequate.

TUMOR SURGERY

As surgery in the treatment of tumors of the head and neck becomes more complete, incidental invasion of the common carotid artery, its bifurcation, or internal carotid artery, does not in itself preclude the abandonment of definitive care. The diseased segment may be removed and a vessel graft interposed. In tumors of the carotid body, it appears justifiable to resect the bifurcation of the common carotid artery if the tumor invades the vessel wall. Some authorities feel that these tumors are not malignant but recurrences following inadequate excision have occurred as well as metastases described. Following the resection of the bifurcation of the common carotid-internal carotid arteries, it is best to re-establish continuity. This will require a vessel graft of an autogenous vein (Fig. 4) or section of external carotid artery which may be transferred as a free graft. Pack and Conley have described external carotid, internal carotid anastomosis following such resections with back flow through the external carotid artery supplying the internal carotid artery. Re-establishment of the natural continuity between the common carotid and internal carotid arteries is to be preferred.

VASCULAR OCCLUSIVE DISEASE

Internal carotid artery thrombosis in the neck usually on an arteriosclerotic basis should always be considered in cerebral vascular accidents. Palpation of the internal carotid arteries often leads to the diagnosis which is confirmed only by angiography or surgical exploration of the diseased vessel. One type of surgical therapy consists of endarterectomy, a longitudinal incision over the diseased area with evacuation of the thrombus. A proximal vascular clamp is

always used. However, recurrent thrombosis is very apt to occur and more recently the surgical treatment is resection of the diseased segment with re-establishment of continuity using a vascular graft. Another technique is a by-pass vascular graft leaving the diseased segment in situ. The basic problem in these latter two methods is whether there is sufficient normal distal vessel at the base of the skull for an adequate arteriorrhaphy.

SUMMARY AND CONCLUSION

All those surgeons who perform major head and neck surgery should be familiar with the basic principles of general vascular surgery. The method of re-establishing vessel continuity either by end to end arteriorrhaphy or by use of a vessel graft should be well known and practiced by all who do any type of major surgery. These techniques and their application have been described in detail.

325 West End Ave.

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LXVIII

FENESTRATION OF THE OVAL WINDOW

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Otosclerosis is a condition in which there is an invasion of the footplate of the stapes by abnormal bone which interferes with the passage of sound from the middle to the inner ear. The surgery of this condition must have as its goal the creation of a permanent passageway for this sound into the inner ear once again.

Without attempting to go into the many techniques already advanced for the treatment of this condition I shall put forth some observations of my own and describe my method of selecting and treating suitable cases.

In the operative treatment of otosclerosis the surgery of the stapes has definite indications and contraindications of its own, which are somewhat different from those for fenestration of the lateral semicircular canal.

PATHOLOGIC PHYSIOLOGY

In otosclerosis the proliferation of the abnormal bone most often begins anterior to the oval window, in the region of the fissula ante fenestrum[1] and is not harmful in itself if it does not invade some vital structure. When it crosses the annular ligament and invades the footplate of the stapes the bone cannot vibrate as it should and hearing loss results. This anterior invasion of the footplate occurs in almost every case and is always deeper and more extensive than the invasion which extends along the superior and inferior rims of the oval window. There is an almost qualitative difference between the two. A small focus of anterior invasion, no more than 10 per cent of the circumference of the footplate, will cause hearing loss. This earliest loss is characteristically more marked for the lower tones, with the slope of the hearing curve upward. Palpation of the head of the stapes demonstrates good mobility except for this anterior

fixation. With the continued invasion of the footplate along the superior and inferior margins this earliest loss increases, generally with the preservation of the ascending slope to the hearing curve. The center of the footplate remains thin and the stapes continues to have fair mobility when palpated on the head. With complete invasion of the periphery of the footplate the slope of the hearing curve becomes flat or descending and even with the most forceful palpation there is no motion of the bone. The comparison of the conductive loss for the lower and higher frequencies is a reliable indication of the extent of footplate fixation. It is inconceivable to me that there is much transmission of sound in the usual manner in such a case. In otosclerosis there must be two simultaneous mechanisms for the transmission of sound from the middle to the inner ear, the first in the usual way, through the vibration of the drum, malleus, incus and partially-fixed stapes. Since this requires the gross motion of the bone, partial ankylosis of the footplate would have more effect on the lower frequences, which have the longer wave lengths, for which there would have to be greater excursion of the bone. For this reason these earliest cases show more loss for the lower tones, with an ascending slope to the hearing curve. The second mechanism of sound transmission is operative but is not too important until the stapes is rigidly fixed by otosclerotic bone. This point is reached when the loss is approximately 40 decibels for air conduction at 256 cycles, when the sound must be 10,000 times normal to reach threshold, and is strong enough to cause motion in the fluid of the inner ear directly, by penetration of the drum and center of the footplate, instead of setting them in motion in the usual manner. Regardless of the amount of fixation of the periphery, if there is no thickening of the center of the footplate the conductive loss at 256 cycles will not exceed 40 decibels. When it does this loss will increase in proportion to the otosclerotic thickening of the footplate.

In addition, after otosclerosis has been present for a number of years there is usually some high-tone perceptive loss from nerve deterioration. Stacy Guild maintains that atrophy of the cochlear nerve is coincidental in otosclerosis and is no more frequent than in the general population.[2] With this I do not agree. I have no statistical evidence on which to make this statement, only the general observation that nerve deterioration is very frequent in otosclerosis. In my opinion the disease we understand as otosclerosis is usually composed of two elements, the growth of abnormal bone which interferes with the vibration of the stapes, and causes the conductive loss, and a later high-tone perceptive loss from cochlear atrophy,

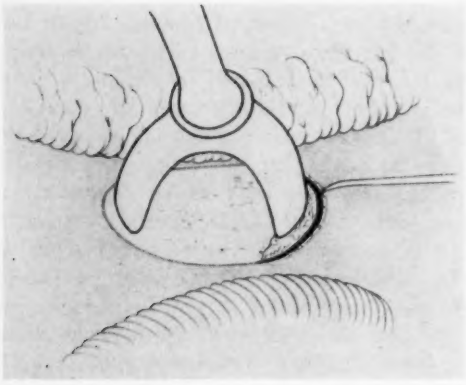
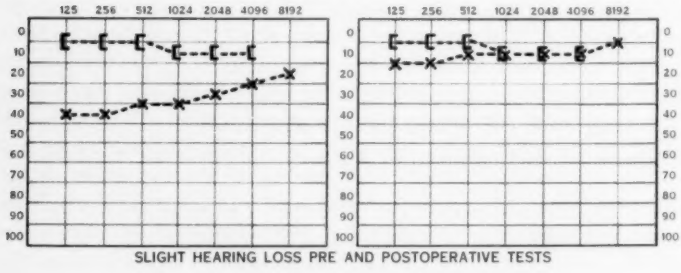


Fig. 1.—Sharp pointed instrument has removed all otosclerotic bone between footplate and oval window to create normal joint space.



FIRST HEARING TEST

which then causes a decreased sensitivity of the inner ear to sound. The perceptive loss is actually independent of the conductive loss, for it may or may not be concurrent with it. There are occasional cases with only a little perceptive loss at 1,000 and 2,000 cycles (the Carhart notch), with advanced conductive loss from such massive otosclerotic accumulation in the oval window as to preclude successful surgery. But in general the high tone loss from nerve deterioration is a late occurrence in otosclerosis, and indicates an advanced state of the disease, with rigid fixation of the footplate by hard mature bone, decreased sensitivity of the inner ear, and a poor prognosis for surgery regardless of how little conductive loss is present. Conversely

the presence of good bone conduction usually indicates a situation that can be improved by surgery.

The amount of conductive loss is, therefore, dependent on the extent of fixation of the periphery and the thickness of the center of the footplate. The perceptive loss depends on the amount of cochlear atrophy and this causes a decreased sensitivity of the inner ear to sound which further magnifies the loss.

This theory of sound transmission does not hold in all cases of otosclerosis, and it must be that in both the first and second mechanisms the hardness of the otosclerotic focus, in addition to its location and extent has an influence on the hearing curve. The hardness of the otosclerosis certainly varies from case to case. The thickness of the center of the footplate is particularly important. Many cases have extensive invasion of the periphery with a thin center, a conductive loss not exceeding 40 decibels, but are very difficult to improve surgically. Cases of otosclerosis can be roughly divided into two groups, those with localized, discrete, hard lesions that can be treated very successfully, and those with widespread, softer otosclerotic invasion that are more difficult to improve. In the latter group an occasional case will have a separate primary focus in the stapes, with complete otosclerotic replacement of the footplate and crurae. There is always widespread replacement of the circumference of the oval window as well, of a slightly different type. Such a case is difficult to improve permanently because of the tendency to reankylosis.

This theory seems reasonable to me, fits the facts as I have oberved them, and is useful in predicting the suitability of cases in anticipating surgery. The hearing test is, after all, a graphic expression of the sound-receptive ability of the ear. By the careful correlation of the hearing test in many cases with the pathologic situation observed at surgery the hearing test can be used to predict very accurately the suitability of a given case for surgery. A method has been developed to record the important information in the patient's history, hearing test, pathologic situation observed at surgery, operative technique used, and the postoperative results on an IBM card. This will be described in a later publication.

GENERAL OBSERVATIONS

1. The less the loss of hearing for air conduction, up to 40 decibels at 256 cycles, the less the fixation of the footplate and the

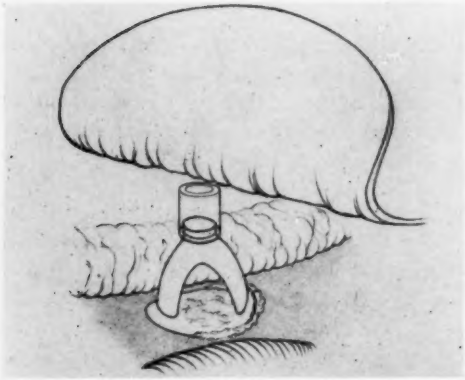
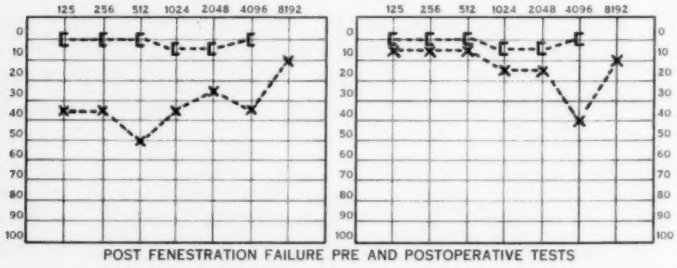


Fig. 2.—Polyethylene 190 tubing over head of stapes to connect it with under surface of drum after removal of otosclerotic bone from around footplate in usual manner in a postfenestration failure case.



more likely the case to be improved by surgery. An ascending slope to the hearing curve, with the air conduction loss at 256 cycles not exceeding 40 decibels is a favorable sign.

2. With more fixation of the footplate there is usually more conductive loss for the higher frequencies and a flat or descending slope to the hearing curve. Even if the footplate is freed at surgery in such a case, which is more difficult to do, it is prone to reankylose because of the more rigid prior fixation.

3. The longer the duration of hearing loss and the earlier in life this loss begins the less likely a good result.

4. It has been observed by Politzer[3] and others that with advanced otosclerosis there is often atrophy of the crura. When this is present there is extensive otosclerotic invasion of the footplate, with loss of the normal nutrition of the crura. There may even be otosclerotic changes in the crura, which can become no more than honeycombs. The audiogram in such advanced cases usually shows a descending curve and as mentioned above this suggest firm fixation of the footplate and weak crura, and a poor prognosis for surgery. These observations are useful in predicting the unsuitability of these cases and as a warning to the surgeon of the fragility of the crura and the consequent danger of fracture with the usual maneuvers for mobilization of the stapes.

INDICATIONS AND CONTRAINDICATIONS

As mentioned previously, I believe the surgery of the stapes has definite indications and contraindications of its own, which are somewhat different from those for fenestration of the lateral semicircular canal.

Indications. Any case of clinical otosclerosis with enough nerve function to hear without a hearing aid if half the conductive loss is removed. The amount of nerve function required will vary, depending on the occupation of the patient. A truck driver can get along with less discrimination than a salesman. As a rule of thumb in estimating gain that can be accomplished by surgery I have found the conductive loss can usually be reduced by half. The amount of hearing loss that can be removed depends in part on the severity of the loss, since more than half of a slight loss can be removed, but usually no more than half of a larger one. In general if halving the air conductive loss does not put the patient at the 30 decibel level for the three speech frequencies, at a point where he can get along without a hearing aid, then surgery is not indicated. The patient wants to hear without a hearing aid, and is generally not interested in an improvement in hearing if he cannot be relieved of his hearing aid. This is an important axiom to remember when deciding on the suitability of a patient for surgery. The better ear is always operated on first. After unsuccessful fenestration has been done the stapes can be operated on in the usual way, and a length of polyethylene No. 190 tubing placed over the head of the stapes and wedged under the drum to rebuild the sound-conducting mechanism.

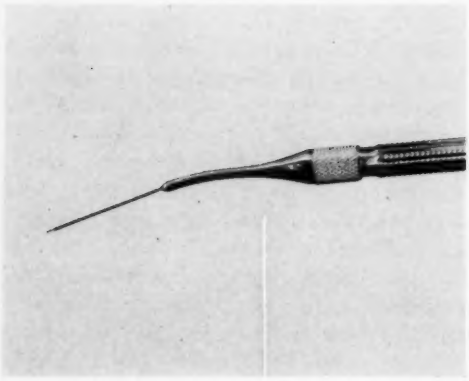


Fig. 3.—Microdrill of Portmann modified to fix onto American handpiece showing curve to reach over anterior crus to site of maximum fixation.

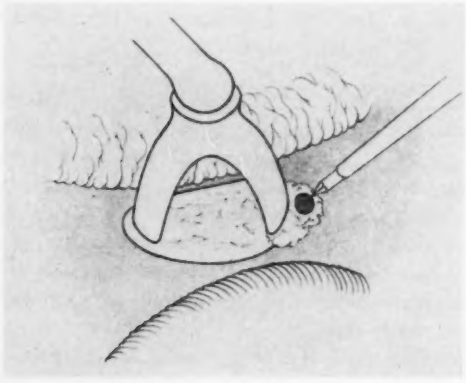


Fig. 4.—Moderate hearing loss showing microdrill hole made in center of anterior otosclerotic focus with penetration into inner ear.

Contraindications. Those patients without enough nerve function to get along in their occupation without a hearing aid if half the conductive loss is removed. It is especially important not to operate on those patients with a steeply-descending hearing test, with poor nerve function at 1,000 and 2,000 cycles, no matter how small the conductive loss. These patients are not going to understand without amplification, even though the hearing be returned to normal

at 256 cycles. They invariably have rigid bony fixation of the stapes, which can be freed only by the most vigorous maneuvers, and no matter how thoroughly this is done they already have decreased sensitivity of the inner ear to sound, and are usually unsatisfactory after surgery because of poor discrimination.

In otosclerosis the perceptive loss can be thought of as causing a decreased sensitivity of the receptor elements of the organ of Corti to the hydraulic stimulation of the pumping action of the stapes. For surgery to be successful when this perceptive loss is present, as in those patients with steeply descending curves, every bit of the conductive interference has to be removed, since the receptor elements are already less sensitive. Unfortunately the bony fixation in these cases is unusually hard and resistant to removal. Because of this regrettable combination of circumstances these patients are much less favorable and should in general be avoided.

The abrupt absence of bone conduction at 2,000 cycles when it is present at 1,000 is a strong contraindication to surgery. Several such patients I operated upon had such massive accumulation of otosclerosis nothing could be done.

I have been disappointed with my results in patients with advanced otosclerosis, with 50 or more decibels of conductive loss for the speech frequencies, who have to use a very strong hearing aid, or who can no longer wear one. I have often found these cases to be beyond any surgical improvement, from massive hard otosclerotic invasion of the footplate mounding up in the oval window, just as one would expect. It does not seem reasonable that one could get a little increase in motion of a stapes rigidly fixed in the oval window. These patients are very subject to the suggestion of improvement, and I believe the reported benefits have usually been wishful thinking. It is a valuable asset to be able to recognize these patients from their hearing tests and explain to them the uselessness of stapes surgery, without having to subject them to it.

Where there is a unilateral conductive loss in addition to bilateral nerve loss, since the conductive element can rarely be completely removed and unless this is done the operated ear will be of no practical assistance and a disappointment to the patient.

SURGICAL TREATMENT

The operation on the stapes I recommend is best called fenestration of the oval window, a direct atack upon the otosclerotic bony

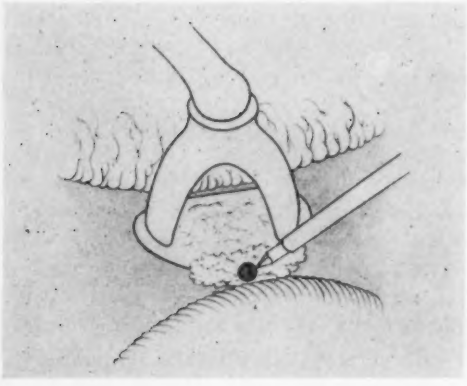
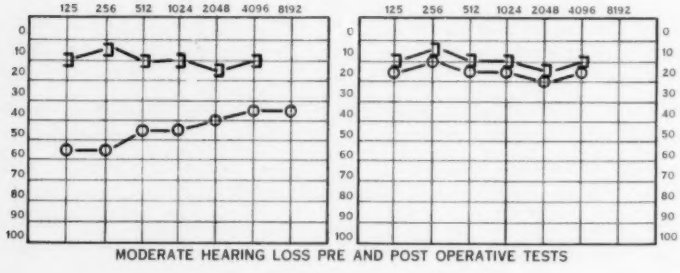


Fig. 5.—Moderate hearing loss showing microdrill hole made in center of inferior otosclerotic focus with penetration into inner ear.



formation, to create a permanent opening for the passage of sound into the inner ear once again. I am opposed to mobilization of the stapes only, since this does not remove the fundamental cause of the hearing loss, the otosclerotic bone, but simply attempts to overcome its result, the ankylosis of the stapes. This is not a matter of terminology, but an important difference in the basic objective of the surgery. I am opposed to forcing the stapes through an exaggerated range of motion, to mobilize it, because I believe the resulting hearing improvement, when achieved, is not likely to be permanent.

GENERAL TREATMENT

1. Heavy preoperative medication, including Thorazine® and atropine for their reflex-blocking actions.

2. Meticulous attention to detail in the operating room with regard to instruments, assistance, darkness, quiet, etc.

3. Comfortable positioning of the patient with a pillow under the back to get the correct arching necessary for good exposure.

4. Zeiss operating microscope for all stages of the operation.

5. Careful clipping of the hair in the external ear, and cleaning of the canal and drum with ether, Phisoderm® and water, and then dusting in Chloromycetin® powder to prevent infection.

6. Infiltration of the circumference of the ear canal with 3 cc of 2 per cent Zylocaine® with ½ cc of 1:1000 adrenalin added.

7. Two straight incisions, beginning about 5 mm from the top and bottom of the drum and meeting at an apex posteriorly, to create a triangular flap which is easier to elevate and bleeds less after surgery.

8. Cautery of the edges of the incision in the ear canal, but never inside the middle ear.

9. Pushing the chorda tympani nerve out of the way, or dividing it when necessary.

10. Generous removal of the bone of the annulus with a small, very tough, stainless steel curette in every case, to get good exposure of the footplate. I use a small burr on the anterior canal wall if it protrudes backward and prevents the use of a large ear speculum.

11. Removal of all adhesions in the middle ear which obscure a good view of the incus and stapes.

12. Careful removal of all bone chips and debris in the middle ear, and perfect hemostasis.

13. Examination of the round window to be sure it is free of obstruction by adhesions or otosclerosis.

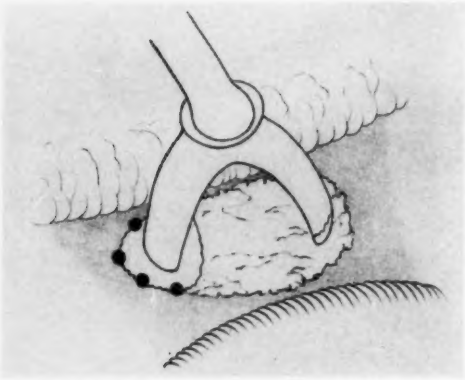
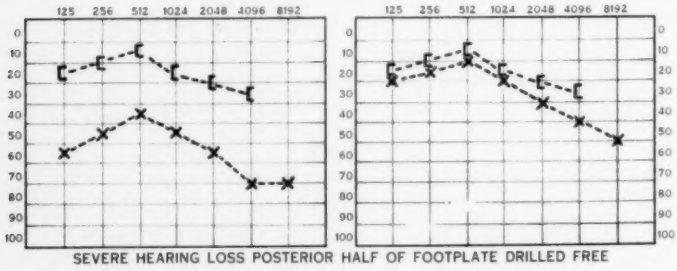


Fig. 6.—Severe hearing loss with massive anterior otosclerotic accumulation in which the anterior crus was fractured and the posterior part of the footplate was drilled free.



FOURTH HEARING TEST

SLIGHT HEARING LOSS

(UP TO 30 DECIBELS FOR THE THREE SPEECH FREQUENCIES FOR AIR CONDUCTION)

1. Inspection of the margins of the oval window, the footplate and crura of the stapes for the characteristic white otosclerotic bone.

2. Gentle palpation of the stapes with a sharp pointed instrument in the cup on the head. Attention is paid to the amount and

direction of the force required and the extent of the motion of the footplate produced.

3. In these cases there is usually no more than a small discrete anterior focus of otosclerosis which can be completely removed with a sharp pointed instrument especially made for this purpose of the toughest stainless steel. This excess bone is completely removed and the joint space between the stapes and oval window is recreated. It is important to penerate all the way through this mass of otosclerotic bone, to get a show of perilabyrinthine fluid, so as to thoroughly free the footplate. It is a temptation in these slight cases to do less than enough. I do not consider I have finished until I can pass the point of my instrument through the joint space from the top to the bottom of the footplate anteriorly without meeting resistance.

4. Gentle palpation of the head then reveals quite a good motion of the stapes in all planes with little or no force.

5. The stapedius tendon is then doubly divided with a special delicate Belluci scissors. This is most important since the tendon may be fibrous or in spasm and both of these situations interfere with the free motion of the stapes.

6. The drum is then put back in place and hearing is tested for air and bone conduction with a 256 cycle magnesium tuning fork struck lightly. The air conduction should be better than bone conduction at this point, and if it is not the drum is pushed forward once again and further surgery done. I prefer this test to the more elaborate testing with the audiometer since it is so much quicker, and in my hands just as reliable. This may be due in part to the heavy premedication I give my patients, which others who do more complete testing do not use. I feel I have done all I can if I reverse the Rinne test at 256 cycles.

7. The drum is then replaced and the two arms of the incision are carefully covered with small pieces of gelfoam soaked in adrenalin. Bleeding rarely occurs postoperatively and nothing further has to be done to remove packing, blood or secretions from the ear.

This same operation can be done on patients who have had previous unsuccessful fenestration surgery by using a short length of polyethylene No. 190 tubing to bridge the gap between the head of the stapes and the under-surface of the drum as mentioned previously.

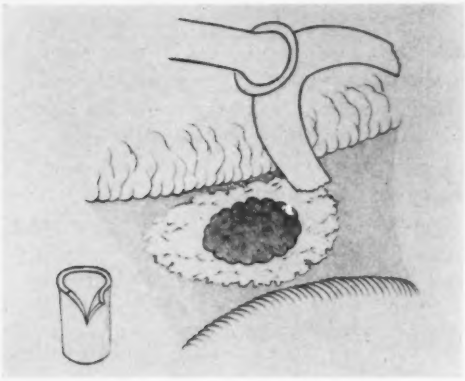


Fig. 7.—Severe hearing loss showing fenestra created in center of footplate and length of vein partially opened.

MODERATE HEARING LOSS

(UP TO 45 DECIBELS FOR THE THREE SPEECH FREQUENCIES FOR AIR CONDUCTION)

1. Inspection of the margins of the oval window, the footplate and crura of the stapes for the characteristic white otosclerotic bone.

2. Gentle palpation of the head with a sharp pointed instrument in the cup on the head. Attention is paid to the amount and direction of the force required, and the extent of the motion of the footplate produced.

3. In these cases there is usually a lot more accumulation of otosclerotic bone, mounded up anteriorly, and extending backward into the footplate, and along the superior and inferior margins of the oval window. There is usually only slight motion of the bone, often no more than impaction of the posterior half of the footplate, with moderate force. The mucoperiosteum is first removed so as to completely visualize the extent of the newbone formation. Here the same removal of otosclerotic bone with the sharp pointed instrument is begun, but it extends too deeply and is too hard to be sufficiently removed by this method. After taking out as much as possible in this way I place the point of the microdrill (modified for the American dental hand piece from the original of Portmann) into the

depression created by the removal of otosclerotic bone from in front of the anterior crus.

This area can be seen in nearly every case, and is the site of the joint between the footplate and the oval window. It is here the otosclerotic invasion of the stapes begins and it is the most important point to be freed to get good motion of the bone, especially that part which accumulates below the level of the footplate in the inner ear and limits the inward motion of the bone. It is a fortuitous circumstance that the one spot that can be seen in nearly every case and can be reached with ease with the specially-curved microdrill, is the critical one to free for successful surgery. With very little effort the otosclerotic bone can be penetrated into the inner ear and after this is done there is usually a surprising increase in freedom of motion of the stapes. It is interesting that there is no increase in motion of the stapes until the drill penetrates into the inner ear and the characteristic clear fluid appears in the drill hole.

Sometimes a little pressure can be exerted on the head in a forward and inward direction and after a definite "giving" inward there is much greater freedom of motion of the stapes. Sometimes a penetration with the drill must be made along the superior or inferior margin of the oval window, or posteriorly, but not often.

These can be easily and safely done if the site of penetration is first prepared by indentation of the bone with a sharp pointed instrument to make sure the drill does not "dance" when rotation begins. The drill is constructed so that no more than 3 mm of the point projects beyond the end of the sheath. In this way no serious injury can be done by the point going too deeply. The microbits are made from a special type of stainless steel that is the toughest and least irritating metal known. With this instrument large accumulations of otosclerotic bone can be removed, and remarkable hearing gains accomplished that would otherwise not be possible.

4. Gentle palpation of the head then reveals quite good motion of the stapes in all planes with little or no force.

5. The stapes tendon is then doubly divided with a special delicate Belluci scissors. This is most important since the tendon may be fibrous or in spasm and both of these situations interfere with the free motion of the stapes.

6. The drum is then put back in place and the hearing is tested for air and bone conduction with a 256 cycle magnesium tuning fork as before.

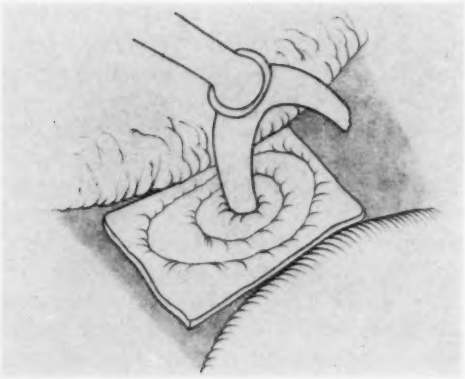
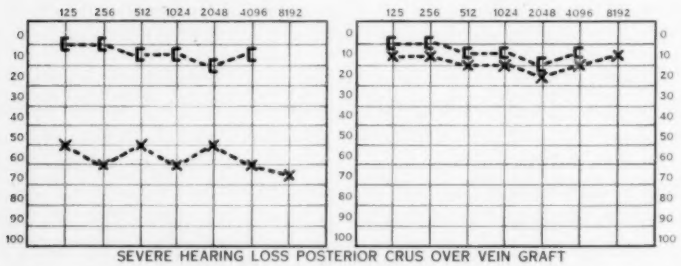


Fig. 8.—Severe hearing loss showing posterior crus in place in center of vein graft over fenestra created in footplate.



FIFTH HEARING TEST

7. The drum is replaced and the two arms of the incision are then carefully covered with a small piece of gelfoam soaked in adrenalin. Bleeding rarely occurs postoperatively and nothing further has to be done to remove packing, blood or secretions from the ear.

I would like to give credit to Dr. Michel Portmann of Bordeaux, France, who, in keeping with the French tradition of medicine, was the pioneer of this definitive method of freeing the stapes and the inventor of the practical drill to make this procedure possible.[4]

SEVERE HEARING LOSS

(OVER 45 DECIBELS FOR THE THREE FREQUENCIES FOR AIR CONDUCTION)

In severe hearing loss the above surgery is usually not sufficient because it is not possible to permanently free the entire stapes when the circumference of the oval window and footplate are replaced by dense otosclerotic bone. Or if the center of the footplate is quite thin the conductive loss may not exceed 40 decibels, but the periphery of the bone can be hopelessly fixed by otosclerotic invasion, and such a case requires more drastic measures than one would expect from the degree of conductive loss alone. Very often these cases are of long duration and have considerable high-tone loss as well and with these clues they can usually be anticipated. In these severe cases some bypass procedure must be done. The discovery by Fowler that a good gain can be accomplished by putting part of the footplate in motion was an important step forward in the evolution of the surgery of the stapes.[5] The following procedure is simply a technical extension of this basic idea that the entire footplate need not be free to achieve a successful hearing gain:

1. Inspection of the margins of the oval window, the footplate and crura of the stapes, which usually show massive invasion and replacement with dense white otosclerotic bone.

2. Palpation of the head of the stapes must be done with the greatest care since just resting the instrument on the head may crumple the crurae. If there is even slight impaction of the posterior part of the footplate with moderate force, then the anterior crus should be divided, and the posterior part of the footplate cut free with the microdrill, similar to the technique described by Fowler. This can be easily done and gives good results.

3. If the stapes does not move at all with palpation of the head, but the center of the footplate is thin enough to penetrate with a sharp instrument or the microdrill, then the crurae are carefully fractured at the footplate and the arch of the stapes is pushed forward out of the line of view. When there is massive mounding up of hard otosclerotic bone in the oval window it is best not to create the fenestra here. Such cases should have fenestration of the lateral semicircular canal, and will not represent more than a small percentage of the cases suitable for surgery of any type. The back of the hand is then carefully prepared and draped for surgery. After

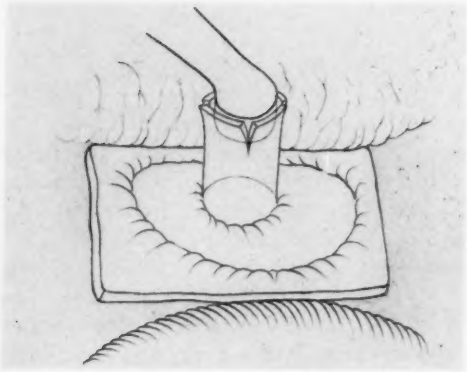
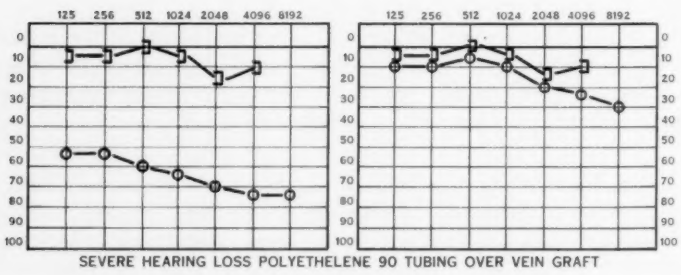


Fig. 9.—Severe hearing loss showing polyethylene 90 tubing in place in center of vein graft over fenestra created in footplate.



SIXTH HEARING TEST

local infiltration of the skin with Zylocaine® and adrenalin a tourniquet is applied to the wrist to engorge the vessels beneath the skin. A 5 mm length of the largest subcutaneous vein is removed. This is carefully freed of fat and cut lengthwise and opened, to be used as a free graft in the ear. It is laid on the promontory with the intima upward since this surface is similar to a mucous membrane and tends to provoke less scar tissue formation. Then with the sharp pointed instruments and the microdrill and special long Shambaugh fistula hooks a fenestra is created in the oval window by removal of as much as possible of the center of the footplate. The loose fragments of bone at the edge of the fenestra are carefully removed

to keep them out of the labyrinth. Care is taken to keep the suction away from the fenestra and no blood is allowed to get into the opening.

The piece of vein is then shifted over the center of the fenestra and carefully invaginated into the opening. The remaining crus of the stapes is then shifted backward into place so that its end is resting on the vein graft over the center of the fenestra.

If the crura have been fractured in a previous operation, or in the attempt to free them from the footplate, a length of polyethylene 90 tubing can be inserted between the lower end of the incus and the vein graft after the remnants of the head and arch of the stapes have been removed. The upper end of this short length of tubing is cross-hatched and spread apart to form a collet to fit over the articular cartilage which remains at the lower end of the incus after the head of the stapes is removed. This makes a tight fit with the lower end of the incus and because it tends to flare outward it would not pass through the fenestra if it were inadvertently pushed inward. By fitting snugly into the cavity of the oval window it is securely fixed in place and does not come loose despite motion of the head.

This fenestration of the footplate and vein graft are really not new, having been presented by me two years ago in slightly different form when I used cutaneous tissue to cover the fenestra and a specially-created plastic stapes.[6] It is the ultimate operation for otosclerosis since it removes the bony obstruction completely and rebuilds the sound conduction mechanism. This is the logical place for fenestration and should theoretically remove all the conductive loss. It is important to understand the operation I described in April, 1956, for which I used the phrase "to fenestrate the oval window," and which is now elaborated upon here is in no way similar to the trephining of the footplate which Rosen later called "fenestration of the oval window."[7] A somewhat similar trephining operation was previously described by Alderton in 1898 without permanent improvement in one patient.[8] It is reasonable to expect that creating a hole in the center of the footplate would increase the sound conduction to the cochlea by the second mechanism of sound transmission, i.e., by direct penetration of the drum and footplate, but it would not be expected to give permanent improvement since such an uncovered hole in the footplate tends to close, as many of us who have tried it have learned to our sorrow. When such a hole is created in the footplate the hearing is better with the drum forward and is reduced when the drum is returned to its normal position, which indicates this is hearing by the second mechanism of sound transmission.

COMMENTS

The surgery of the stapes is the direct method of relieving conductive hearing loss in otosclerosis. Fenestration of the oval window as described here is occasionally more time consuming and difficult than fenestration of the lateral semicircular canal, but it is initially more successful, and I believe it will be more permanent. It is certainly less annoying to the patient than fenestration of the lateral semicircular canal.

Anatomic factors are important in results of this surgery, since the procedures on the footplate require adequate exposure which may not be possible to obtain. Sometimes the footplate is obscured by an overhanging facial ridge or promontory, or abnormal displacement upward or backward and these factors can preclude successful surgery. The greatest usefulness of this operation is in the slightly and moderately hard of hearing in which thorough cleaning of the margins of the oval window can be accomplished with a sharp pointed instrument and the electric microdrill. The bypass operations described are still in the developmental stage, but the initial results have been very encouraging and only time will determine their permanent value. For those many patients who have already had unsuccessful mobilization of the stapes surgery, even perhaps with a great decrease in the hearing, this new vein graft technique is particularly important.

SUMMARY

I have presented some observations of my own on the pathologic physiology of otosclerosis and the surgery of the stapes. I do not believe that all cases of otosclerotic hearing loss should be attempted by this method. A new concept of this surgery is advanced with illustrative cases.

1018 Madison Ave.

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LXIX

THE SURGICAL RESTORATION OF HEARING IN CHRONIC OTITIS MEDIA AND ITS AUDIOLOGICAL BASIS

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The task of restoring the function of the middle ear in chronic otitis media by way of surgery involves four problems: 1) of pathological anatomy, 2) of clinical otology, 3) of audiology, 4) of plastic surgery.

Since these operations have to assure a definitive cure of the disease process before restoring function and, therefore, require that the plastic operation be combined with a thorough revision of the whole middle ear, I have described them as "tympanoplasties." The methods of tympanoplasty are adapted to every degree of destruction of the middle ear and can nearly always, even in the case of an infected ear, be carried out in one stage. In this way more of the particular structure and also of the function of the middle ear can be preserved. The indication for tympanoplasty, therefore, is not dependent of the condition which the middle ear presents, whether it is a defect with almost no inflammatory irritation or a mucopurulent or fetid secretion, a polypoid inflammation or a cholesteatoma with either a large marginal defect and secondary migration into the tympanic cavity or by way of proliferation of the epithelium from the flaccid membrane into the epitympanon almost like a benign tumor assisted by inflammatory irritation, as reported by Rüedi.

In the otosclerotic disturbance of function an operative solution for a distinct pathological problem the ankylosis of the stapes had to be found. In chronic otitis media, on the other hand, a combination of various pathological processes exists, among which inflammatory and otosclerotic fixations of the stapes also occur. Thus tym-

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From the Department for Ear, Nose, and Throat Diseases of the University in Würzburg.

Read before the Sixth International Congress of Otolaryngology in Washington May 6, 1957.

panoplasty was charged with the task of solving quite a number of different pathological and functional problems. It has been so much developed in the meantime, that it is basically capable of responding to any given task.

The clinical problem is, from the point of view of classical otology, a simple one if the middle ear in question is practically free from inflammation, but it becomes difficult when suppuration or cholesteatoma formation supervene. Even by radical mastoidectomy in all its various forms have we been unable to remove every trace of inflammation and secretion from the mucosa of the tympanic cavity and eustachian tube. But so long as the destruction in the middle ear, especially of the ossicles, has not progressed so extensively as to necessitate the removal of the malleus and incus, radical mastoidectomy implies an unnecessary sacrifice of an important part of the middle ear, the epitympanon. Without the presence of a closed epitympanic space the covering of the ossicles with a skin graft will be followed by adhesions and displacements which will severely impair the functioning of the chain. Viewed from the audiological angle the epitympanon with the ossicles could theoretically stay open, provided a tympanic membrane of good quality has been re-established by means of a skin graft. Clinical experience however shows that this method is so imperfect as to make it unpractical because the soiling and infection around the ossicles leads to secretion from the epitympanon. Even if a closure of the mesotympanon has been spontaneously established by means of membranes extending from the tympanic membrane to the facial nerve it frequently does not prove to be strong enough to withstand the pressure of middle ear inflation or serous otitis media. Every infection of the middle ear may lead to renewed protracted secretion and proliferation of the mucous membrane, i.e., a recurrence of the chronic otitis media, and eventually abolish the audiological result.

In those cases showing a proliferating infection of the mucous membrane in the epitympanum, healing cannot be accomplished by a two-stage operation in which the bridge, as well as the malleus and incus are being preserved, because infection continues between the two operations, with the formation of adhesions. Only by opening up the narrow spaces in the epitympanon and filling them with a mixture of antibiotics and cortisone in a one-stage procedure, and the early inflation of the whole tympanon, does the mucous membrane in the epitympanum have a chance to heal and to form the free air spaces again. For these reasons the tympanoplasty is almost always a one-stage operation in which the pathological condition of the middle ear

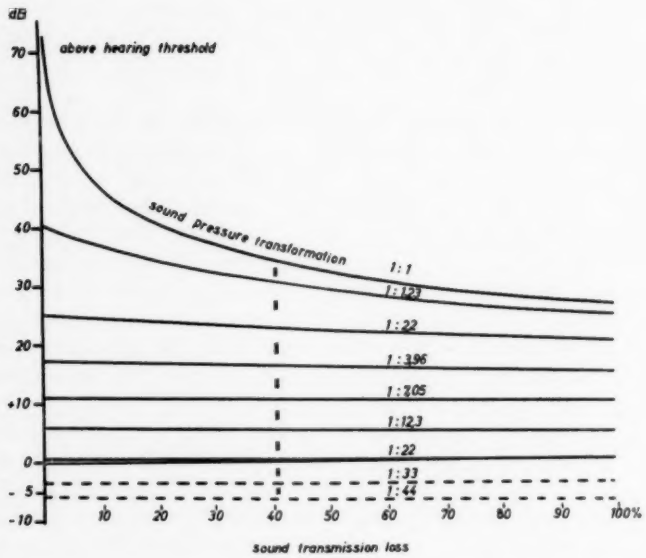

Fig. 1.—Increase in the threshold of hearing with altered sound pressure transformation in relation to sound transmission loss of the tympanic membrane or its substitute. Ordinate: increase of threshold in db, Abscissa: sound transmission loss in percentages. Pressure transformation and F factor by which the normal pressure transformation changes (1:22) are altered, are designated.

is healed and functional reconstruction is accomplished at the same time.

Closure of a middle ear affected with chronic suppuration is contradictory to principles of surgery and in particular plastic surgery which should be carried out only in a healed area, free of infection, and is at variance besides with the notions and rules of otology, as we have known them until now. I should have hardly been the first to shoulder the responsibility for this method of treating otitis media in a one-stage operation followed by closure of the infected tympanon, had it not been for the fact that I had devoted 15 years to an intensive study of labyrinthitis and labyrinth osteitis. In all tympanoplasties the surgeon must examine every section of the middle ear for signs of disease with the operation microscope and make provisions for their absolute healing. In such circumstances even a

labyrinthine fistula forms no contraindication. A long time ago I described the surgical method for the exploration of the whole middle ear without disturbing or destroying the functional structure in a well preserved middle ear by 1) an opening to the antrum and the aditus ad antrum, 2) through Shrapnell's membrane to the epitympanon, the ossicles and oval niche and 3) to the round niche and to the hypotympanon. I have also shown it on film. The matrix of the cholesteatoma must with every one of its processes be entirely removed under the guidance of the microscope. If the ossicles are still preserved but already completely overlaid with matrix in the epitympanon, there is unfortunately no prospect of replacing this matrix after its laborious removal with mucous membrane. But without a complete lining of all surfaces with sound mucosa no new open tympanic cavity is possible. Just as in the case of severe adhesion processes so in this situation malleus and incus must be removed. It is, however, the very aim of these preserving and restoring operations to operate for cholesteatome so early that a sacrifice of this kind becomes unnecessary. Since a certain number of cholesteatomata are to be regarded as nonmalignant tumors, early tympanoplasty is particularly apt to remove in the earliest stage the epidermis which is derived from the embryonic auditory lamina and give rise to this tumor-like development, and to replace it by a skin graft.

Provided that the function of both fenestrae is unimpaired, the audiological problem in tympanoplasty resolves itself in the task of restoring the necessary sound pressure difference between the two scalae of the cochlea in order to restore the inner ear hydrodynamics and thus the stimulation of the organ of Corti. In this respect the transformation of sound pressure upon the oval window by the tympanic membrane and the ossicles and the sound protection of the round window by the tympanic membrane are decisive. The principle of sound pressure transformation is known to us since Helmholtz, its effect consisting, according to a calculation by v. Békésy, of the relation between the footplate of the stapes and the tympanic membrane = 1 : 17 (according to Wever and Lawrence, 1 : 14) and the lever action of the ossicles (according to Damann) = 1 : 1.3 and thus amounting to = 1 : 22 for the whole sound pressure transformer. Conversion into db, as has been published earlier by myself, gives 24.6 db for the tympanic membrane as pressure transformer, 2.3 db for the ossicles, a total of approx. 27 db. Assuming a breadth of variation in the relationship between stapes and tympanic membrane as from 1 : 15.5 to 19.5 and of the lever action as from 1 : 1.2 to 1.5, there results a variability only of 3 db in the whole pressure transformation.

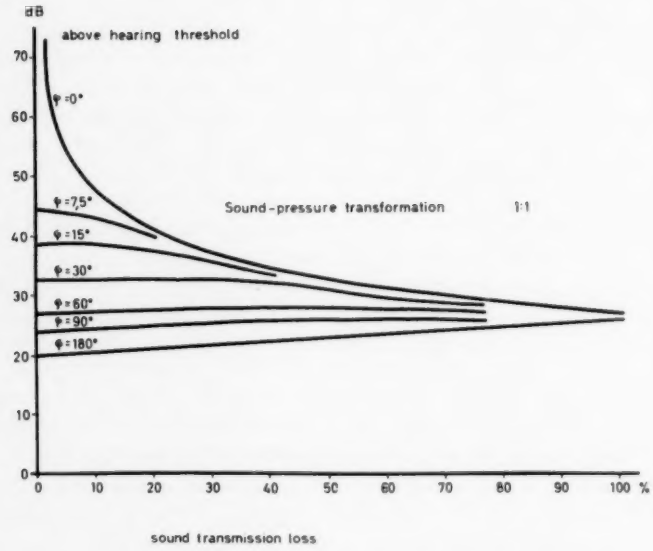

Fig. 2.—Increase in the threshold of hearing relative to sound transmission loss and phase displacement (without any sound pressure transformation). Abscissa: sound transmission loss in percentages. Parameter: phase displacement.

Theoretically we can regard the tympanic membrane as having a twofold action, namely, that of a pressure transformer and that of a sound protector and also in actual practice it is possible to divorce the two functions by a method of fenestration, by which I manage to preserve unaltered the whole structure of the middle ear and in particular the tympanic membrane. With progressive deterioration of sound pressure transformation up to its complete loss, the acoustic threshold rises, given 100 per cent sound protection, to 27 db. This sound protection consists physically of two components, i.e., sound transmission loss and phase displacement. The more the one regresses, the stronger grows the action of the other (see below).

A reduction in the sound protection from the ideal 100 per cent by 25 to 30 per cent means only a loss of 2.5 to 3 db, as the following diagram, the computation of which I owe to my collaborator, H. G. Schmitt, shows. The 30 db line of the fenestration, i.e., hearing without sound pressure transformation, is therefore reached with a sound protection of about 70 per cent, which is to be regarded as optimal.

A lowering of sound protection from 100 per cent to 50 per cent means a loss of 6 db, to 25 per cent a loss of 12 db, and to 10 per cent a loss of 20 db. If we add to this low sound protection of 10 per cent, representing 20 db loss of hearing, the loss of another 27 db, caused by the lack of sound pressure transformation, a reduction in hearing capacity of 47 db will result. Thus an increase in sound protection in its higher degrees affords only a small gain, but quite a decisive gain its its low degrees (see diagram).

If both windows are equally accessible to the sound pressure, no pressure difference and therefore no stimulation of the inner ear arise. However, as we know from clinical experience, the acoustic threshold lies in fact between 45 and 50 db, when a complete defect of the tympanic membrane obtains. Solely the topography of the wall of the promontory, i.e., the shape of the round niche affords in this lower part of the curve already a sound protection of up to 10 per cent perhaps by way of a sound shadow effect of the niche. In the presence of a tympanic membrane giving 70 per cent sound protection, however, the round niche offers an additional protection of only 10 per cent of the remaining 30 per cent of sound pressure in the tympanic cavity, i.e., 3 per cent or approximately ½ db in this upper part of the curve. The shape of the wall of the promontory makes it at all possible to hear without a tympanic membrane; with an intact tympanic membrane the shape of the round niche is insignificant.

Hearing by means of an increase of sound pressure upon the oval window, i.e., by means of sound pressure transformation, is always more effective than hearing by means of a reduction in sound pressure in front of the round window, i.e., by sound protection, even if the pressure transformer is of a much reduced effectivity, as will also be seen from Diagram 1. If sound pressure transformation of even moderate degree is available, sound protection, i.e., occlusion of the tympanic cavity is audiologically no longer necessary. From the point of view of surgery a free graft can only then heal securely serving as a new tympanic membrane, if it is offered a nutritional basis on its whole circumference and a good support. The whole system of eustachian tube and middle ear cannot be clinically definitively healed, unless the new formed middle ear is completely closed.

From the diagram it can be seen that hearing with 10 db loss can be achieved with a pressure transformer, the effect of which is reduced to about 1/3 with 15 db to about 1/5 with 20 db even to 1/10, in the latter instance with a threshold which under most favor-

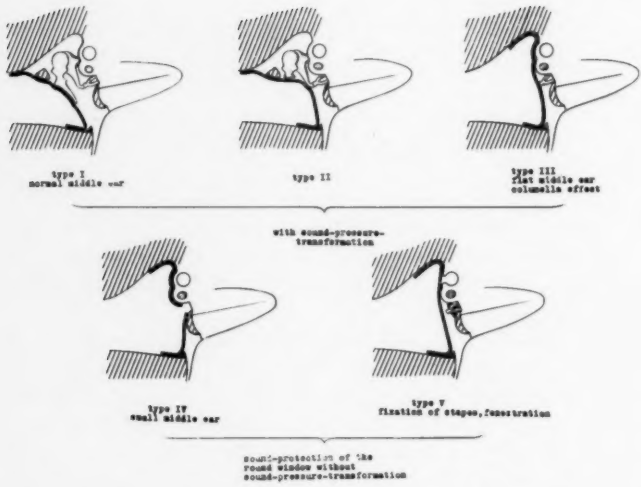

Fig. 3.—Type I: Normal tympanic cavity. Type II: Partial defect of the ossicular chain with sound pressure transformer. Type III: Shallow tympanic cavity, columella effect. Type IV: Small tympanic cavity, sound protection of round window without sound pressure transformer. Type V: Fixation of stapes, fenestration.

able circumstances can also be achieved by protection and phase displacement. All these values refer only to a sound protection of 70 per cent (any great variation of which is almost without significance if good pressure transformation obtains).

From an audiological point of view, the reconstruction of a partial sound pressure transformation will always exceed the optimal sound protection. From this fact it becomes understandable that I tried to provide a new sound pressure transformation by means of an artificial columella when there were defects in the crura of the stapes. This technique is especially helpful in cases in which there is danger of adhesions and scars forming in the oval window niche from pathological causes, in which, without the artificial columella, not even the result of a proper sound protection could be reached.

Each effect of the middle ear which results in a noticeable hearing gain is dependent on those two factors, pressure transformation and protection. Each degree in the combination of destruction of these

two factors can be calculated (according to the equation [H. G. Schmitt] which is the basis of Figure 1) following the equation

$$y = \log \frac{22}{22 \times F - P}$$

Sound protection is a combined effect of sound transmission loss and phase displacement. The normal tympanic membrane with its pressure transformation must be able to vibrate (in which case the effect of sound protection becomes unnecessary), i.e., it must up to a degree be pervious to sound. Apparently no physiological investigations into this exist, although the impedance of the tympanic membrane similar to that of the air would make one expect permeability (Groen). During the passage of a vibration through a membrane a phase displacement occurs (Broemser) which, in the case of hearing with sound protection only, raises the difference in pressure between the oval and round windows. When hearing with a healthy middle ear, sound protection is, because of the strong rise in pressure through transformation, almost insignificant. After fenestration, however, the result rests on the sound protection afforded by the almost (or, according to my method) completely unaltered tympanic membrane; a larger perforation will at once undo the gain in hearing. The effect of sound transmission loss of a membrane acting as sound protector is greater the more inert it is, i.e., if it is very slack and its mass large (e.g., whole skin grafts in tympanoplasty) and vice versa.

The improvement of hearing through phase displacement reaches its maximum at 180°, i.e., factor 2, representing 6 db after conversion. Sound transmission loss and phase displacement are interdependent. With 100 per cent sound transmission loss there is no phase displacement. Because of the gain of 6 db being based on a 100 per cent sound transmission loss, the effect of the phase displacement may give a gain in hearing greater than 6 db as the sound transmission loss decreases (Fig. 2, H. G. Schmitt). A more favorable gain in hearing can be obtained with a 50 per cent sound transmission loss combined with 180° phase displacement than with complete sound transmission loss (Fig. 4).

From these results it can be concluded that in all surgical procedures to improve hearing if adequate sound pressure transformation has been provided for sound transmission loss and phase displacement are almost irrelevant. If however the sound pressure transformation decreases considerably the effect of sound transmission loss will assert

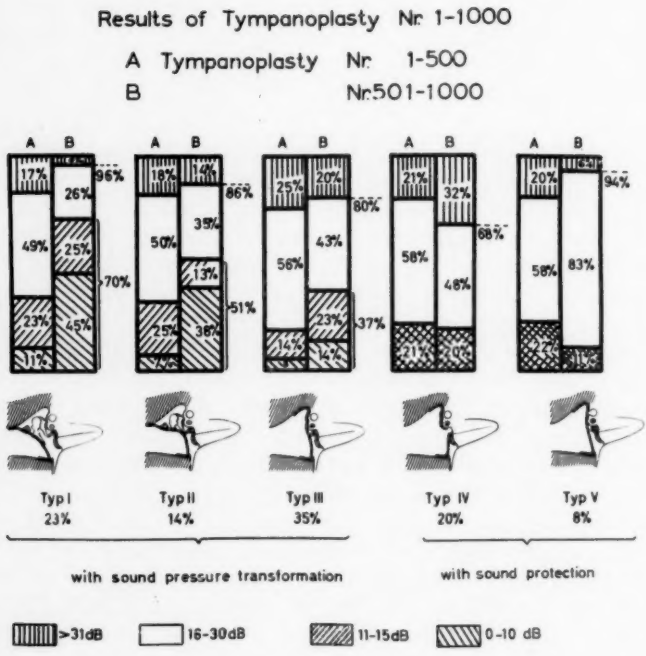

Fig. 4.—Tympanoplasty. Air bone gap after operation.

itself more and more. Phase displacement gains in importance the more sound transmission loss declines.

The more important among the other factors are the sound absorption of the tympanic membrane, the resonance frequency of the middle ear system (apart from the external ear) and a directional effect of the ear cavity.

Only the sound energy which has been absorbed by the tympanic membrane is for sound pressure transformation effective. In the case of a healthy middle ear its optimum is, according to Menzel, between the frequencies 500 - 3000 Hz and amounts to over 75 per cent. A lowering of absorption by a free skin graft or a scar within small limits is only of little moment; the decrease from 75 per cent to, say, 50 per cent will cause only approximately 3.5 db loss of hearing.

Since the middle ear system is composed of the resonance-frequencies of the various part systems and the damping effect of these systems is large, there is no pronounced resonance peak but only a slow decline of the acoustic threshold above the resonance-frequency. It is important that the resonance-frequencies should not decline too far towards 2000 c.p.s., because word intelligibility would be impaired by such a lowering of the threshold curve. According as to whether a graft is to act as pressure transformer or protector, its qualities must be of a different kind. The resonance-frequency of the sound pressure transformer is high, if its mass is kept sufficiently small and its elasticity high. In some particularly favorable results of sound protection (especially in type IV of my classification) with a wide open oval niche, in addition to resonance a certain direction effect towards the oval window is surely involved, as was assumed also by Tonndorf.

In deciding the method of tympanoplasty to be applied, factors derived from audiology, clinical otology and surgical technique will have to interact and be adapted to the degree of the defect in the middle ear. All forms of audiological operations on the middle ear can be fitted into my five types of tympanoplasty and are applicable not only in otitis media chronica or tympanosclerosis but also in injuries and benign tumors of the middle ear, atresia of the auditory meatus, in which according to the extent of the malformation any of the five types of tympanoplasty may be required. Fenestration in ankylosis of the stapes belongs to type V, mobilization to type I, and they are audiologically quite different (Fig. 3).

The problem of plastic surgery in chronic otitis media consisted at first in the task to reconstruct a new air-filled tympanic cavity by replacement of the defective tympanic membrane. This problem I solved by using free skin grafts and provisionally filling the tympanic cavity with a reabsorbable substance; only then could details of the technique for the different types of tympanoplasty be evolved. I have always drawn skin for the free full thickness skin graft from behind the ear, as is generally customary nowadays, because this skin is almost free of glands and hairs and its corium contains only few elastic fibers and, therefore, neither shrinks nor curls up. The provisional filling of the tympanic cavity forms the basis for the freely over the middle ear extended graft and keeps it viable during healing. During this time it gradually liquefies and becomes partly absorbed or flows outwards through the tube. Recent animal experiments of my collaborator Kley have shown that pure gelatine sponge, thoroughly saturated with penicillin and hyaluronidase, causes no reaction

on the part of the mucosa and provokes no adhesions. The healing of the infection and the diseased mucosa is also facilitated. If, however, a new adhesive process develops in spite of these precautions, the blame for it does not belong to the gelatine filling but to the gravity of the pathological process in the mucosa which extends into the submucosa and periosteum.

The factors governing indications, surgical methods and results in tympanoplasty are, as viewed according to their audiological and surgical importance, the following:

1. State of the spiral organ of Corti.

2. Function of the auditive tube.

3. Function of both fenestrate, a) fenestra rotunda, b) fenestra ovalis or nov-ovalis.

4. State of the mucosa, first and foremost in the hypotympanon and tube, then in the mesotympanon and finally the epitympanon.

5. Quality of the remains of the tympanic membrane.

6. State of the ossicles.

In chronic otitis media there are functional disturbances in the area of both windows, or only the fenestra rotunda, much more frequent than in otosclerosis. Since the round window cannot be replaced by a new one in a distant place of the labyrinth as can the oval window, and lies in all types of tympanoplasty within the new tympanic cavity, restoration of faultless hydrodynamics on the side of the scala tympani and ventilation through the hypotympanon are urgent matters. For this the preservation and healing of the mucosa in the tympanic cavity and particularly in the round niche are decisive and are, if defective, replaced by me with a Thiersch graft from lip mucosa (previously amniotic membrane). The audiological curves which were shown above, explain why the results after skin grafting in total defects of the tympanic membrane very often approximate normal hearing. The formation of a new tympanic cavity succeeds, however, more easily, if a large part of the collagenous layer of the tympanic membrane and of its mucosa still remains. Preservation or defect of the ossicles decide whether a type of operation with sound pressure transformation or with sound protection has to be performed; in any case an improvement of hearing capacity by surgical means is possible of attainment.

I have published over many years typical results of the various tympanoplasties, carried out even in severest middle ear suppurations. Today I present only the statistics relating to 1,000 operations, the results having now reached a certain uniformity. These results are classified as I consider it as useful: they are regarded as good in all operations with sound pressure transformations and a conduction loss of not more than 15 db, with sound protection alone of not more than 30 db. In case of sound pressure transformation and a conductive loss between 15 and 30 db they can be regarded as only fair. This classification is simple and appropriate for both groups (Fig. 4). As our interventions are only able to diminish the conductive loss of the deafness, the comparison of the air-bone gap before and after the operation demonstrates the effect of surgery better than speech audiogram can do it.

A small part of the second group with sound protection only can also achieve 15 db, after all sources of error of practical audiology were taken into consideration. But these cases do not really correspond to the results of the first group with pressure transformation, among whom many retain less than 10 db and even 5 db of middle ear component, which does not happen in the second group. In type III the disease of the middle ear in the majority of cases is too severe to allow of such good results in a high proportion of patients. All these operations can have such favorable results only because hearing in the middle ear rests on a few factors, which are either taken advantage of by nature for this purpose or else remain without significance (compare again Figure 1).

UNIVERSITATS HALS-NASEN-OHRENKLINIK

LXX

PATHOHISTOLOGICAL AURAL CHANGES IN THE PROGENY OF A MOTHER WITH PSEUDOHYPOPARATHYROIDISM

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Albright, Burnett, Smith and Parson,[1] in 1942, described a pathological condition, naming it pseudohypoparathyroidism. In 1950 Elrick, Albright, Bartter, Forbes and Reeves[4] defined this entity with greater precision. The disease is very rare, and the extant cases were reviewed, in 1954, by Macgregor and Whitehead.[7]

In pseudohypoparathyroidism the abnormal chemical findings exist in the presence of hyperplastic parathyroid glands. Bartter[3] remarked as late as 1956 that nothing is known about the etiology of the disease. Relationship to achondroplasia and myositis was stressed. Parathyroid extract given intravenously does not produce phosphaturia, and it fails, also, to lower the serum phosphorus or to raise the serum calcium. No glomerular insufficiency is present. Demonstration of parathyroid tissue by biopsy makes the diagnosis definite. A hereditary factor has been suggested. Cases became known where several members of a family were afflicted,[6] or where the condition was recognized in mother and child.[10] Several times the disease was present in two sisters.

Metaplastic islands of true bone are found in skin and connective tissue, besides changes in the bones of the extremities. Macgregor and Whitehead saw placques of calcium on the face, hands, abdomen and auricle. The ear tophus consisted of calcium phosphate with organic protein. In subcutaneous calcified placques actual bone formation was seen. Eaton and Haines[3] noticed symmetrical calcification in the basal ganglia. Reynolds, Jacobson, Edmondson, Martin and Nelson[8] reported unusually high intracranial calcification. Bone changes and calcifications can be present together or either of them alone.

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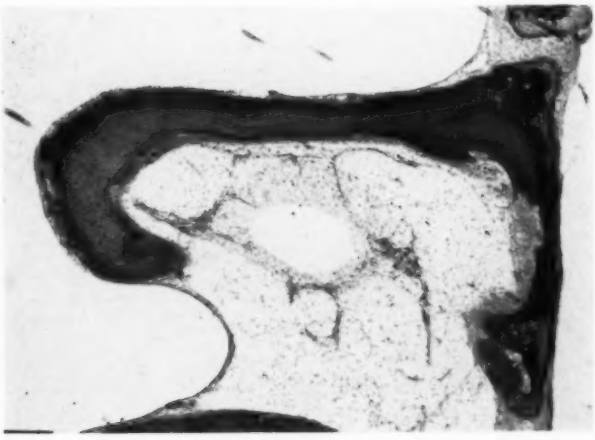

Fig. 1.—Hematoxylin-eosin, x250. Stapedial niche; obturator foramen filled with mesenchyme. In the center location of the obliterated stapedial artery marked by a condensation ring. Center of the bony stapes plate: thinned out ad maximum by a granulation mass.

Symptoms do not appear under the age of two years, and are then discovered by development of calcific nodules in the skin. Mental deficiency has been found to be the rule.

REPORT OF A CASE

The 26 year old white single woman was studied from the age of 17. Her history forms Case II in the publication of Elrick, Albright, Bartter, Forbes and Reeves of 1950, to which inquiry concerning details must be referred. Very obligingly, Dr. P. H. Henneman prepared the following short summary of the history:

The patient was first seen by Dr. Albright in 1948 at the age of 17 because of low intelligence, short stature, short fingers and toes, and sleepiness. Studies revealed a serum calcium of 6.0 mg %, phosphorus 6.1 mg %, alkaline phosphatase 2.9 B. U. %. X-rays showed short metacarpals and metatarsals and subcutaneous ossification. There was no response to administered parathyroid extract. Thus the patient fits the syndrome described by Albright under the name of pseudohypoparathyroidism. These patients have histologically normal parathyroid glands, but fail to respond to their own hormones.

Classically they have associated short stature, short metacarpals and metatarsals and subcutaneous ossification.

The patient was started on treatment with Vitamin D which raised her serum calcium and lowered her serum phosphorus. At the time of her delivery in 1956, she was taking vitamin D 400,000 units daily and 0.9 gm calcium lactate daily. On this dose of Vitamin D her serum calcium and phosphorus were essentially normal throughout her pregnancy. On the day of her delivery her serum calcium was 8.9 mg %, phosphorus 5.9 mg %. Cord blood calcium was 12.9 mg %, phosphorus 8.9 mg %.

An acute middle ear infection with purulent discharge, suffered in childhood in her left ear, had resulted in a slight hearing loss in this ear. At examination the right tympanic membrane was found to be retracted and scarred in its posterior half; the left tympanic membrane retracted with scars in the posterior and inferior quadrant. Weber was lateralized into the left ear. Audiometry, in the year of her delivery, revealed normal hearing in the right ear, and in the left ear a loss of 30 decibels at 512.

Her pregnancy was uncomplicated. The baby, born at term by a low forceps delivery, was well developed, well nourished, with a weight of 2680 gms and a crown-rump length of 33 cm. Resuscitation was very difficult, and respiration became spontaneous only after 45 minutes. After another 45 minutes of spontaneous breath with pure O_2, the heartbeat and respiration suddenly failed.

The immediate cause of death was designated as cerebral congestion and edema due to maternal pseudohypoparathyroidism. Dr. K. Benirschke, pathologist to the Boston Lying-in Hospital, planned to publish the details of the pathological investigation, and thanks are due to him for the release of the right temporal bone for otohistological examination. In his report the auricles are described as formed and placed normally. His summary reported minimal microscopic cerebral calcifications and endochondral bone formation which was remarkable in that the zones of provisional calcification were narrow and the chondroblast nuclei persisted within the calcifying cartilage.

The specimen contained the inner ear inclusive of the promontorial wall and the stapes and parts of the petrous pyramid. After decalcification and celloidin embedding 600 sections were obtained in a vertical plane; they were stained with Delafield hematoxylin and eosin, Heidenhain-Mallory, Gomori impregnation, and with acid

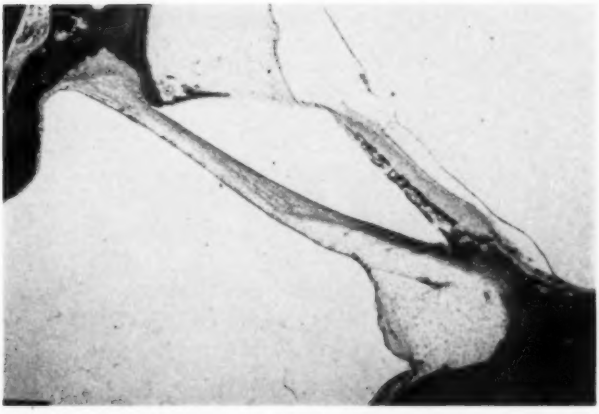

Fig. 2.—Hematoxylin-eosin, x35. Niche of the round window filled with mesenchyme; in one corner hyaline mass grown together with the round window membrane.

fuchsin according to Eros (1928) to demonstrate calcium in decalcified bone.

The petrous apex was diploic without attempts at pneumatization. The niche of the oval window (Fig. 1) was filled by connective tissue interspersed with fibroblasts. Similar tissue filled the niche of the round window (Fig. 2), with a hyalin block placed against the lateral one-third of the tympanic surface of the membrane of the round window. Rosenthal's canal was well filled, and the membrane of Reissner was in normal position. The organ of Corti was poorly preserved; however, the elevation of its mound testified to its being normal. The end organs of the vestibular labyrinth were normal.

Several remarkable features were offered in this sectional series. In the obturator foramen of the stapes a loose mesh of connective tissue with bipolar fibroblasts represented remnants of the mesenchyme; in the center an opening was left (Fig. 1) surrounded by a ring of condensed mesenchyme fibers. This opening corresponded to the location of the stapedial artery, which itself had disappeared long ago through obliteration in the course of normal development. The internal acoustic meatus contained psammomas (Fig. 4). The enchondral layer of the cochlear capsule showed a nearly completed developmental stage. In fully one-half of the sections (Nos. 5 to

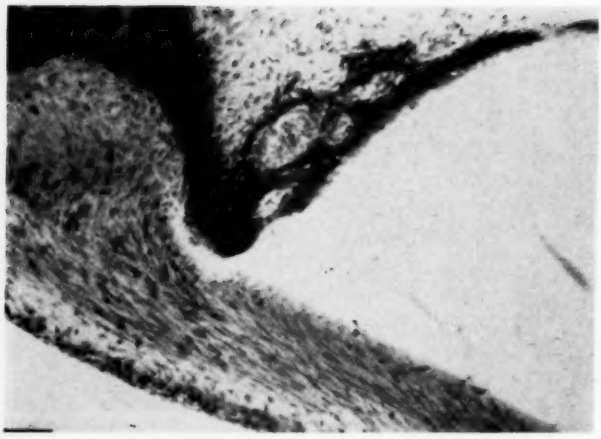

Fig. 3.—Hematoxylin-eosin, x180. Calcifications along the epithelial surface of the spiral ligament and around the vessels in the ligament.

310) calcifications were observed in the spiral ligament (Fig. 3). Their location was such that either the inner surface of the spiral ligament was lined by the deposit or the latter surrounded the arteries near the basal end of the ligament. The vessels were not thrombosed, and the calcium formed a cuffing around them. The calcifications in the basal section of the spiral ligament were restricted to the area of the basal turn, while the deposits within the vascular stria were seen at the level of the basal and the middle turn.

COMMENT

Although symptoms of this disease are said to appear under the second year of life, here the abnormal calcium deposits were already present at birth. They corresponded to findings of calcification in the central nervous system.

The enchondral layer of the cochlear capsule was well on its way to definite formation, but it is only with caution that this stage of development can be declared as precocious.

Rollin[9] reported three cases with calcium deposit in the vascular stria (in two children, 2½ and 6 years old respectively, and in a male of 59 years); the deposits appeared in a hearing organ without further

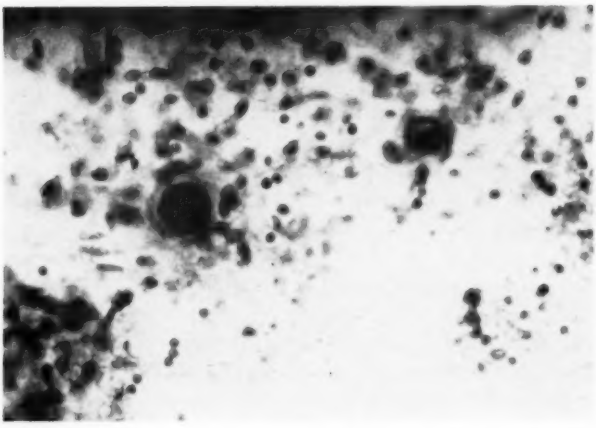

Fig. 4.—Hematoxylin-eosin, x150. Corpora amylacea in the internal acoustic meatus.

signs of pathology. Rollin considered the calcifications to be the result of a dystrophic process analogous to the development of the psammoma bodies or corpora arenacea from endothelial elements gathered in clumps and undergoing hyalin degeneration, with parallel processes being observed in the arachnoidal granulations of Pacchioni.

Although the corpora amylacea are normal histological features in the internal acoustice meatus according to Waltner,[12] they may have some pathological relations as postulated by Rollin. The latter quoted M. B. Schmidt,[11] who found already in the first year of life calcareous deposits in the walls of the plexus arteries. In the present case the calcium-cuffed vessels were not thrombosed; on the other hand it is impossible to state how far their lumen had already become constricted.

In our collection of sectional series of temporal bones, slight deposits of a similar nature were found in several cases of otosclerosis, Paget and toxoplasmosis. All these are known to represent disturbances of the calcium metabolism. However, in decalcified bone the search for this condition is accompanied by technical difficulties; extreme caution is indicated and the problem warrants a more comprehensive approach.

Fischer[5] enumerated the artifacts most frequently seen in the spiral ligament, adding that it is not too difficult to differentiate between varieties like the compact and the edematous, loose ligament and the artifacts.

How far the abnormal calcium metabolism in pseudohypoparathyroidism is able to create in the hearing organ changes that influence its function remains to be seen, also the role of the altered central nervous system in the production of similar functional disturbances is yet to be determined.

In the present case, a conspicuous granulation mass in the center of the stapedial plate (Fig. 1) left merely a very thin layer of the bony wall still standing and obviously near to disappearance. This being one of the changes pointing to abnormalities in bone formation, respectively reabsorption, the critical location of this focus arbitrarily demands attention. Although the blocking of the labyrinthine windows in the present case could well result in congenital functional losses, this condition is all too common to draw conclusions from it at this early period.

SUMMARY

In the ear of a term newborn of a mother with pseudohypoparathyroidism of many years' duration, calcifications were found in the spiral ligament inclusive of the vascular stria, together with corpora amylacea in the inner meatus. The center of the stapedial plate was found in full reabsorption by a granulating focus. These changes paralleled calcifications in the central nervous system as signs of a disturbed calcium metabolism present extensively through many years in the mother.

With its possible influence on the later development of the hearing organ, this rare condition could furnish one of the hitherto unrecognized causes of congenital deafness.

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LXXI

THE STABILITY OF THE COCHLEAR RESPONSE THROUGH TIME

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Since the discovery of the Wever-Bray[3] effect in 1930, the electrophysiological technique of recording the cochlear potentials has been utilized widely in studies of auditory reception. This technique yields valuable data concerning the properties of various elements of the ear.

In many experiments in physiological acoustics, experimental manipulations produce effects upon the ear which are reflected in changes in the magnitude of the cochlear potential. Frequently some arbitrary output obtained under controlled conditions is employed as a reference, and the effects of experimental conditions are measured as deviations in output from this reference. At once the question arises as to the suitability of such a reference because it is clear that accuracy in the measurement of experimentally induced effects depends heavily upon its stability.

It is known that the cochlear response generated by a constant stimulus (of 0.5 dyne/per square cm or less) is itself constant over short periods of time. But constancy over more lengthy periods has yet to be demonstrated. Because the complexity of experiments in physiological acoustics demands them, often many hours are required in order to complete these experiments. Accordingly, it is important to know whether or not the cochlear response is stable under prolonged stimulation. It should be apparent that absolute constancy is unlikely because of the natural variability of the physiological processes, which influences the cochlear response. Changes in the physiological state of the preparation can produce alterations in the magnitude of the cochlear response which are independent of

those changes produced through experimental manipulation, and this is so even though the stimulus is maintained without variation.

In the present study, inquiry was made into the stability of the cochlear response through time. By learning the extent of variation in output of the response under conditions of constant stimulation, an estimate of error of measurement could be made. The prolonged stimulation afforded an opportunity to observe any possible change that such stimulation might have upon the cochlear potentials. Techniques of maintaining physiological preparations could be assessed. Cats were used as experimental animals.

PROCEDURE

Animals were anesthetized with a solution of diallyl-barbituric acid and ethyl carbamate which was injected intraperitoneally in a dosage of 1 cc per kilogram of body weight. Each cc of this solution contained the following: 0.1 gm diallyl-barbituric acid, 0.4 gm ethyl carbamate, 0.012 gm sodium hydroxide, and distilled water, q.s. The hydrogen-ion concentratoin of the solution was slightly alkaline (pH 8.0). Administration of the anesthetic preceded surgical operations by about 30 minutes.

Adequate ventilation was provided by tracheal cannulation.

A mid-line skin incision on the ventral surface of the throat provided access to the trachea. The sternohyoid and sternothyroid muscles were cut by electrothermal cautery, and a small transverse cut in the ciliated epithelium and connective tissue between two adjacent tracheal rings provided entrance for the cannula.

The tympanic bulla was approached laterally through an oval incision in the skin covering the parotid gland. This incision was in line with the coronoid process of the mandible and the base of the pinna. Division between two ligatures of the superficial temporal vein gave access to the parotid gland which was then elevated to expose its blood supply. This supply was ligated and the gland removed. Resection of the sternocleidomastoid, digastric, and stylohyoid muscles and removal of the periosteum exposed the bulla. Entrance by drilling through the bulla made the round window membrane accessible for placement of a recording electrode.

A closed bulla technique was employed. Two holes were drilled in the lateral surface of the bulla: one hole (diameter 2 mm) was

located near the stylomastoid foramen, just ventral to it, to accommodate the wire from the active electrode; and a second hole (diameter 5 mm) was located in an anterior position toward the jugular foramen to serve as an inspection hole during electrode placement. Through this hole the round window could be seen clearly. Both of these holes were closed with tightly fitting rubber stoppers. Through the smaller stopper passed a fine hollow tube which insured equilibration of air pressure within and without the bulla cavity. The closed bulla technique was utilized in order to minimize the possibility of a reduction in the recorded response due to an accumulation of serum or other fluids on the round window membrane.

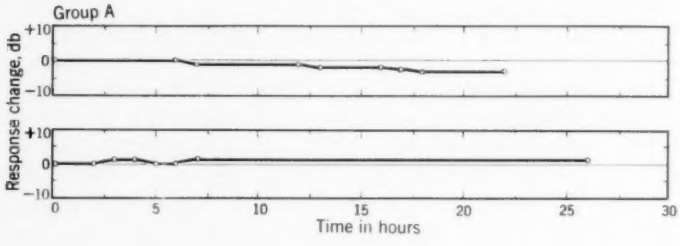

Fig. 1.—Changes in the magnitude of the cochlear response through time with constant stimulation (continuous 1000 cycle tone). Changes are indicated in db relative to the initial level established at the onset of stimulation.

The active electrode consisted of a piece of platinum foil which was soldered to the end of a nylon coated copper wire. An inactive electrode made from a steel hypodermic needle was inserted into the superficial layer of the masseter muscle.

The stimulus was restricted to a 1000 cycle tone produced by a beat frequency oscillator. The signal from this oscillator was connected through a filter and an amplifier to a Daven attenuator (Type T-690 CR) with a range of 100 db, variable in steps of 1 db. Output from the attenuator fed into a power amplifier which drove the speaker (Western Electric 555 receiver). Aerial sound was conducted into the ear by a tube leading from the speaker. A cannula on the end of this tube was inserted into the external meatus and tied securely, thus providing a closed acoustical system.

Cochlear potentials picked up from the round window membrane were amplified and then measured with a wave analyzer (General

Radio, Type 736-A) operated as a selective voltmeter. Each experimental animal was isolated in an electrically shielded soundproof room.

Two different procedures were employed for the maintenance of experimental preparations. For Group A the procedure involved no more than the regulation of the temperature in the experimental room (84 degrees Fahrenheit). For Group B, however, the procedure involved attempts to maintain each preparation in as constant a physiological state as was feasible. Intramuscular injections of epinephrine were employed to stimulate the heart: tissue hydration was maintained within normal limits with periodic peritoneal injections of 2½ per cent dextrose in saline; and the level of anesthesia

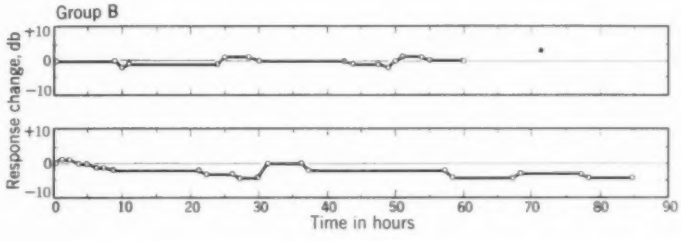

Fig. 2.—Changes in the magnitude of the cochlear response through time with constant stimulation (continuous 1000 cycle tone). Changes are indicated in db relative to the initial level established at the onset of stimulation.

was kept from wide fluctuation with supplementary intramuscular injections of pentobarbital sodium (Nembutal®). The level of anesthesia was sufficiently high to allow positive pinna and corneal reflexes to tactual stimulation. When necessary, a urethral catheter was used to expedite urinary clearance.

RESULTS

Changes in the magnitude of the cochlear response for two representative cats from Group A are presented in Figure 1. Changes in output are given in db relative to the initial level established within the first few minutes of recording. One preparation showed a slow progressive loss which amounted to 3 db after a 22 hour period. The

other preparation fluctuated (1 db) through the first six hours, and then remained stable through an additional 20 hours.

Data for two representative cats from Group B are presented in Figure 2. Once again, changes in output of the cochlear response are represented in db relative to the initial level. Both preparations demonstrated a slow and progressive loss in output during the first 20 hours. Thereafter, the magnitude of the response varied around the reference level (1 to –4 db) for as long as 65 additional hours. For each of the preparations depicted in Figures 1 and 2 further observations were prohibited by death.

COMMENT

Data from this experiment indicate that the cochlear response is stable through prolonged periods of continuous stimulation. Typically, changes in the magnitude of the response resulted in small losses of a few db. In several preparations, however, the changes were of fluctuation around the initial output level. In no instance was a progressive gain noted. No preparation gained more than 1 db and none lost more than 4 db. Considering the fact that several preparations sustained cochlear responses within these limits for longer than three days, the response seems suitable as a referent. As a qualification to this statement several interesting observations should be noted.

Apparently the cochlear response is relatively independent of gross physiological changes since procedures employed to maintain preparations had no material effect upon either the maximum output level or the stability of the response. However, more than any other single thing, body temperature seems to have played an important role in maintaining the response. With several preparations, warming the body (not the head) restored a loss in the response and kept it from further change for the duration of the experiment. This effect is probably due to improved circulation and not to significant changes in the temperature of the cochlea itself.[1,2,4]

On two occasions losses in the recorded response were found to be due to excessive fluid on the round window membrane. Removal of the fluid restored the cochlear potential to its initial level. On subsequent preparations in order to reduce seepage around the rubber stoppers, the operative field was packed with an absorbent hemostatic dressing (Oxycel®).

Data from this experiment indicate that prolonged stimulation at low intensity levels (below 0.5 dyne/per square cm) does not significantly impair cochlear potential output.

PRINCETON UNIVERSITY

From the Princeton Psychological Laboratory. This work was supported by a contract between the Office of Naval Research and Princeton University Nonr 1858(18) and by Higgins funds allotted to Princeton University. Permission is granted for reproduction and use by the United States Government.

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LXXII

A CONSIDERATION OF SOME PHYSIOLOGICAL PRINCIPLES IN THE SURGICAL TREATMENT OF MÉNIÈRE'S DISEASE

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The process of recovery from the vertigo produced by the sudden loss of one vestibular labyrinth is not well defined. It is known however that a person who has received a direct insult to the labyrinth with the consequent incapacitating vertigo may in a matter of hours to weeks experience re-establishment of equilibrium and equanimity. Hallpike recognizes this process as a central one and proposes that it is entirely a function of the vestibular nuclei, stating that: "If the right labyrinth be destroyed, then the unopposed tonic impulses from the left labyrinth will cause rotation of the head to the left with nystagmus to the left. As we know, this nystagmus, severe at first, gradually disappears in the course of a few weeks, its abolition being brought about by a process of central compensation. Thus the right vestibular nuclei being deprived of incoming tonic impulses, set up a rhythm of their own, and in this way the output of the two sets of vestibular nuclei are once more brought into balance and nystagmus ceases."[1]

Hallpike was undoubtedly speaking of the pigeon in referring to the rotation of the head because this does not occur in man. Man receives the preponderance of neck muscle tonus from the cerebellum. The pigeon receives most of its tonus from the vestibular nuclei, and loss of neck muscle tonus on one side results in head-wagging movements (Kopfbewegungen).

There are major objections to Hallpike's explanation of the restoration of vestibular balance, objections which are based upon practical physiologic considerations and known principles of central nervous system physiology.

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First, if balance is attained through readjustment solely in the involved vestibular system, one would expect the activity of the opposite labyrinth to be unaffected. However, this is not the case. It is usual for the caloric response in the normal ear, after successful destructive labyrinthotomy, to revert from normal to marked hypoactivity. If it is hypoactive pre-operatively, the response is, for all practical purposes, absent after cessation of postoperative vertigo and nystagmus. (It is interesting that even with totally absent response to maximal caloric stimulation postoperatively, these patients have not the difficulty walking in the dark one might expect, as in patients with vestibular streptomycin toxicity. Is it possible that vestibular efferent fibers are here operating much in the manner of the postulated cochlear efferent fibers, to produce suppression?) The process of recovery would then seem to involve both vestibular systems, the key process being suppression of the opposite system rather than excitation of the first system.

Secondly, it is not likely that a system as complex as the vestibular apparatus can undergo major alteration without involving many higher neuron arcs in that alteration. The central nervous system, reduced to its simplest terms, is a huge system of receptors, transmitters, and way-stations, arranged in interdependent units, each with its complement of regulatory fibers. Regulatory fibers may be excitatory or inhibitory. It is these latter fibers that are of great importance in vestibular suppression.

Vestibular suppression is developed to a high degree by figure-skaters. Their ability to execute 20 or 30 continuous, violent spins and stop suddenly without post-rotatory nystagmus, staggering, or other signs of disorientation is well known, and is dependent entirely upon suppression of responses from their normal vestibular centers.[2] Ballet dancers spin at a much slower rate and avoid post-rotatory vertigo by "spotting" or maintaining a constant reference point in their field of vision.[3]

If restoration of equilibrium after destructive labyrinthotomy is brought about through suppression of the opposite center, as seems likely, higher centers would be involved. Cranmer[4] demonstrated some of the principal tracts producing inhibition of vestibular nuclei. The cerebellar cortex has connections with the nucleus fastigius, suppressing the effect of the nucleus fastigius on the lateral vestibular nucleus of each side. The nucleus fastigius itself is booster to the lateral vestibular nucleus on its own side and suppresses that on the opposite side. Thus, increased cerebellar inhibition applied to the

appropriate vestibular center will tend to restore equilibrium and diminish nystagmus. A double set of inhibitors, pyramis and fastigius, is hereby brought into play.

The vestibular nuclei also have connections to the pre-occipital and occipital cortex. The parietal and probably also the frontal cortex participate: the conscious will for equanimity is brought to bear through the great inherent ability of the central nervous system to compensate for a faculty lost.[5]

After central suppression has occurred, the opposite labyrinth when stimulated, even though discharging through its suppressed vestibular system, may be considered as adding to the imbalance, thus producing nystagmus. The breakthrough, however, will not be major if the compensatory mechanisms of the central nervous system have been efficient. Vertigo will not occur. This ability of the central nervous system is, of course, a function of many things—time, age of the patient, efficiency of the CNS vascular supply, absence of intercurrent disease, and the vigor of the whole organism.

A case report may be illustrative. In the literature of the last twenty years we have not found a similar case documented to demonstrate this principle.[6]

REPORT OF A CASE

The patient, a 49 year old man, was first seen at the University Hospital with the chief complaints of tinnitus, deafness, and recurrent nausea and vomiting. Significant in the past history was the occurrence of a skull fracture 39 years previously. Since that episode, which made him bedridden for three weeks, he had been totally deaf in the right ear. He gave no clear-cut history of vertigo at that time. Ten weeks before coming to the hospital, while he was in the mountains, he experienced a roaring tinnitus in his left ear upon awakening. Late that day he first noticed decreased hearing in that ear which by the following day left him handicapped. On the second day he was constantly nauseated and he began vomiting. This seizure lasted longer than a week. For several days he noticed a mild degree of left lateropulsion, but at no time noticed vertigo, lightheadedness, giddiness, or other variety of dizziness. Then for two weeks he was well except for moderately severe deafness which showed some gradual improvement subjectively. Loud noises bothered him constantly.

In the fourth week of his illness he again noticed a sudden decrease of his auditory acuity, increase in tinnitus, and immediate

nausea and vomiting. This attack lasted three days and was again accompanied by slight left lateropulsion but no dizziness. Following this episode his hearing did not improve.

General physical examination and objective otolaryngological examination were not remarkable. Pure tone audiometry revealed a rather uniform 50-60 db perceptive loss in the left ear. He could not hear a loud shout on the right with the left ear properly masked. Tests with the Bekesy automatic sweep frequency audiometer confirmed the pure tone findings, and demonstrated what is considered to be recruitment on the left. Aural overload testing[7] revealed markedly diminished linear range of hearing in the left ear. This was in the neighborhood of ten db. The normal range is 45 to 65 db.[8] Restricted linear range of hearing by overload testing is believed to be an indication of cochlear disease. Caloric testing with 25 ml of ice water produced no nystagmus on the right and a hypoactive response on the left (1st and 2nd degree nystagmus lasting fifteen seconds). Testing with 25 ml of warm water produced no response on the right and again, a hypoactive response on the left. Faradic and galvanic labyrinthine testing produced no response on either side (conjugate deviation of the eyes).

The patient was given a seven-day course of intravenous histamine therapy and was discharged on the Furstenberg regimen with nicotinic acid. A month later he had one subsequent seizure lasting one day. This attack was preceded by a definite feeling of improved hearing.

This case meets the criteria set forth for Ménière's disease with but one exception: the subjective symptom of vertigo is absent. The patient undoubtedly had involvement of both the cochlear and vestibular compartments of his left inner ear. Cochlear signs (decreased linear range of hearing, recruitment, and distortion) were manifest and abundant. Vestibular signs also were present: slight lateropulsion, nausea, and vomiting. The stimulus to nausea and vomiting is effected through fibers from the medial vestibular nucleus through the medial reticular gray to the dorsal efferent nucleus of the vagus nerve and the reticular gray in its vicinity, producing autonomic imbalance and reverse peristalsis.[9] Nausea and vomiting are vestibular and not cochlear manifestations. In Ménière's disease without vertigo, that is, cochlear deafness, which Williams[10,11] as well as Wright[12] and others have described, cochlear signs are present but vestibular signs are absent. Many of these patients do develop vestibular signs later in their disease, but develop vertigo as well.

The above case, then, is not the Ménière's disease without vertigo as defined by Williams, Wright, and others.

The case apparently typifies a new variety of Ménière's disease without vertigo, in which the vestibular compartment is truly involved in the disease process but does not give rise to vertigo. This is because a cortical appreciation of the sensation of vertigo must have as its basis an uncompensated and unsuppressed neurophysiological imbalance between two actively discharging vestibular systems. A labyrinthine crisis involving an acclimated vestibular system discharging against a nonfunctioning contralateral labyrinth is probably not stimulus sufficient to summon into the conscious mind a major sensation of disorientation in space. Vertigo will not be present. The surgeon then has no hesitation in assuring his patient freedom from vertiginous seizures after destructive labyrinthotomy for unilateral Ménière's disease if central compensation has occurred. Even if Ménière's disease subsequently develops in the opposite ear, though cochlear and vestibular disease is present, vertigo will not be a feature. This will not be a common occurrence, but it is of tremendous psychic benefit to the patient to have this assurance. Day[13] in 1943 reported 220 cases in which he had performed a destructive labyrinthotomy for Ménière's disease. He stated that in only one patient did Ménière's disease develop in the unoperated ear following surgery, and that there was only cochlear involvement which was controlled by medical treatment. Since Ménière's disease with cochlear involvement alone comprises less than ten per cent of all cases of Ménière's disease, it is possible this patient may have had classic Ménière's disease but without vertigo, on the basis of the process described above.

SUMMARY

After the loss of one vestibular end organ, re-establishment of equilibrium and equanimity is gained through a combination of inhibition of the active vestibular system and compensatory development of the remaining healthy units of the central nervous system. A case of what probably was classic Ménière's disease with vestibular involvement but without vertigo is presented in illustration of this neurologic concept. In this case, the presence of a "dead" inner ear opposite the diseased ear is thought to have provided the basis for the neurologic process. An understanding of this process can be of use in the surgical management of Ménière's disease.

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LXXIII

A NOTE ON THE MEASUREMENT OF NASAL FLOW RESISTANCE

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The recent appearance of two papers, only four months apart, on the measurement of nasal flow resistance represents a revival of interest in this subject after a period of almost 20 years. In 1939 Scheideler[7] had reported on such a method and in 1940 Uddstroemer[11] on a different one. Now (1958) two new methods are being offered by Seebohm and Hamilton[8] and Semerak.[9]

The current concept of nasal air flow is largely based upon the classical writings of Proetz.[4] The present writer, because of some work of his own on nasal aircurrents (1939),[10] became interested in the two articles under consideration in the course of his duties as a reviewer. However, the mere reporting in the form of conventional abstracts did not permit a critical evaluation of the merits and of the limitations of such methods and this the writer felt was needed for the clarification of certain points.

First, a brief classification of methods for the assessment of nasal flow resistance may be indicated. These can be divided into two broad groups: 1) functional assessment; 2) quantitative measurement.

An example of the first group is the well known Glatzel mirror which allows the observer to see whether or not there is a difference in patency on the two sides of the nose. Also in this group belongs the method of Uddstroemer. The latter author determined the percentage of air passing through the nose in relation to that passing through the mouth by means of gas flow meters. Both methods may be of help to the surgeon in assessing the need for surgical correction, the use of the mirror being much simpler and therefore likely to be preferred. As was recently pointed out by Proetz,[5] these relatively gross methods combined with simple inspection are sufficient for most surgical purposes.

However, in allergic rhinitis, alteration of nasal patency (or resistance) is much more subtle and therefore requires more exact methods of measurement. The mere observation of the degree of congestion, color of the turbinates, amount of secretion present is helpful but hardly allows for a quantitative assessment of the changes under the effect of therapy. Here is where quantitative measurement may have its place as was suggested by Seebohm and Hamilton. Their own method and that of Semerak belong to this group (in addition to that of Scheideler) and since both use essentially different principles they must be briefly reviewed here.

Seebohm and Hamilton introduced a pair of small tubes into the pharynx through the mouth. Through one of these tubes a small amount of air was released at a predetermined flow rate while the patient was requested to shut his mouth tightly over the tubes and also to close his glottis so that all air was forced out through the nose. The second tube was connected to a pressure registering device which read the differential pressure re. that of the surrounding air. This way a record was obtained of the pressure alterations induced by the air flow. Incidentally, this method is similar to that of Scheideler, the only difference being that Scheideler sucked the air into the tube placed into the nasopharynx, simulating inhalation instead of exhalation as did Seebohm and Hamilton. With Scheideler's method the tubes have to be placed very carefully (topical anesthesia is often necessary), lest the soft palate be sucked into the tube.

Semerak's approach was different: his measurements were taken while the patient breathed regularly. A pneumotachograph was inserted firmly into one nostril for measurement of the instantaneous flow rate. The contralateral nostril was closed off by another insert which was connected to a manometer (no flow took place on this side). The manometer then gave the instantaneous pressure value which under the conditions described may be taken as that in the nasopharynx. Both flow rate and nasopharyngeal pressure were registered continually by a photokymograph.

The first reaction when comparing both methods might be that the use of the patient's breathing as in Semerak's method may be considered better from the physiological point of view. However, insertion of a stiff connector into the nostril partially off-sets this seeming advantage. Such an insert may deform a long and slender nostril and help to stiffen relatively soft alar cartilages. Thus the source of increased nasal resistance is eliminated by the instrument which is supposed to measure it. Insertion of a connector into the

nostril is not so objectionable as some writers seem to assume because it might alter the direction of the inhaled air stream, at least not as long as the direction is not changed to an extremely steep or flat angle. Proetz[5] has recently called attention to this point.

The difference between both methods would be rather unimportant if nasal resistance were a simple function of the air pressure in the nasopharynx and of the flow rate as is expressed in Ohm's law:

$$R = \frac{p}{i}$$

(R - resistance, p - pressure, i - flow rate)

It would be obvious and has in fact been assumed so by Semerak that measurement (or predetermination) of p and i would render a value of R which would be valid generally. However, the application of Ohm's law to the problem of nasal air currents is limited for reasons of aero-dynamics. At low flow velocities (i < speed of sound) flowing air behaves like an incompressible medium, that is, like a fluid. Therefore, the hydrodynamic laws are directly applicable as they were first postulated by Daniel Bernoulli in 1738. Additions pertinent to the present problem were made later by J. L. M. Poiseuille (1840) and by O. Reynolds (1883).

Poiseuille had stated that Ohm's law is true only as long as one is dealing with a laminary flow. However, as soon as eddying (or turbulence) sets in, the flow pressure (the pressure need to move a given column of air or liquid at a given flow rate) becomes proportional to the square of the flow rate. Reynolds then had derived an index number composed of the product of the diameter of the passage, the flow velocity, and the viscosity of the fluid (or of the gas). This Reynolds number is small for laminary flow, whereas eddying (and eventually turbulence) set in when this number exceeds a value of 1160 (but is smaller than 10,000).

(Since some writers are apparently confused on these two terms, it may be remembered that an eddying flow is defined as an event in which vortices are either continually present or are formed periodically; in other words the event is still a well defined motion. Turbulence, however, is an entirely random motion about which only statistical statements can be made such as the average velocity, etc.)

This writer (1939) has calculated the Reynolds number for a normal human nose and for quiet respiration (16x/min) and found it to be approximately 1000. This means that the airflow is still

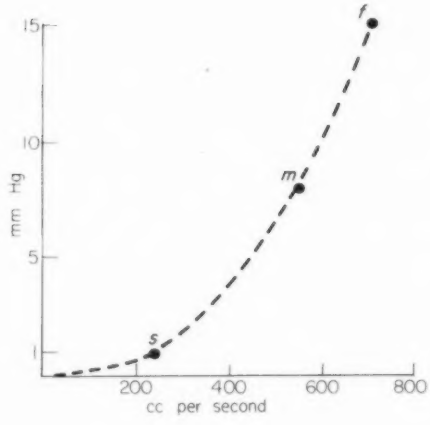

Fig. 1.—Flow rate vs. pressure in a normal nose for three different breathing rates (s - shallow, n - normal, f - forced). The plotting has been prepared from Semerak's records which are continuous recordings of changes in flow rate and in pressure over several breathing cycles.

laminary, but being close to the borderline (1160) probably not very stable. This theoretical result was confirmed by subsequent experiments. It was observed that eddying made its appearance under a variety of conditions a) when the breathing rate was only slightly accelerated; b) when the cross-sectional diameter was altered in some section of the passage-way either aa) by narrowing, e.g., by making the middle turbinate hypertrophic, or bb) by widening, e.g., in an atrophic nose; and c) each time when the direction of flow was reversed, even during normal respiration, i.e., when inspiration was relieved by expiration or vice versa.

Quantitative evidence for the non-linear dependence of pressure upon flow rate can be derived from the results of Seebohm and Hamilton and of Semerak. Figure 1 has been plotted from Semerak's published data for the normal nose under three different conditions of breathing (shallow, normal, and forced). Nonlinearity is clearly

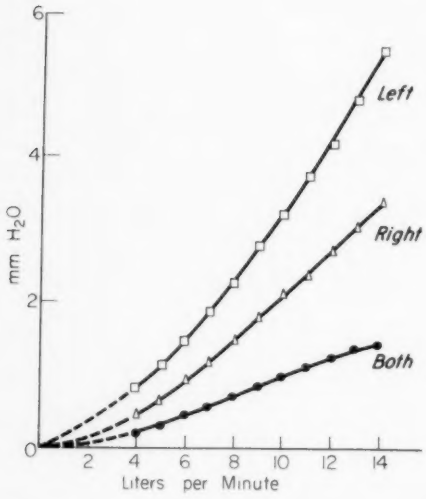

Fig. 2.—Nasal flow rate vs. pressure in one subject. Right - rt. nostril which was slightly stuffed-up when the record was made; Left - left nostril (normal patency); Both - both nostrils open simultaneously. From unpublished data of Seebohm and Hamilton.

indicated. Figure 2 has been made available to this author from unpublished data of Seebohm and Hamilton. In this plot again nonlinearity is present, most pronounced in the example of the slightly stuffed-up nostril (i.e., the more resistant).

Actually, the pneumotachograph as used by Semerak is a device in which laminary flow is insured by subdividing the flow channel into a large number of narrow tubes (Semerak used up to 61 tubes in one of his instruments). Determination is made of the pressure drop over a given distance along one of the tubes. For conversion of these pressure differentials Semerak calibrated his pneumotachograph for known flow rates. His calibration charts show a) a nonlinear relation between the pressure in the calibrating system (the latter was measured in a large bottle to which the pneumotachograph was connected) and the flow rate and are b) different for the two flow directions, i.e., inspiration and expiration. These results indicate that even though flow was laminary within the measuring device, eddying within other parts of the complex system under consideration had its effect upon the results obtained.

For reasons of this nonlinearity it becomes necessary to know at which part of the p vs. i function the reading in a particular subject was taken. Seebohm and Hamilton used predetermined flow rates which from this point of view turns out to be an advantage. In Semerak's case, both parameters, p and i were obtained by measurement, that is, they were largely independent of the observer's control. The following alternatives present themselves in the opinion of the present writer. In Semerak's method where a running record of pressure and flow rate values are made as they alter with the respiratory cycle, one could integrate the curve pertaining to the flow rate by means of a planimeter. This way the volume of inhaled (or expired) air per breathing cycles would obtain and this volume could be made a more meaningful basis of comparison between subjects. It is noted in this respect that volume and flow rate are not always proportional to each other since in cases of forced breathing, especially through narrow noses, the flow rate curve becomes highly complex as is attested by Semerak's own results.

Another, perhaps simpler way of solving this problem, and this applies to both methods, would be to measure a larger number of "normal" noses at varying rates of flow (or breathing rates respectively) and thus to establish a standard curve for pressure vs. flow rate. For pathological noses, one would have to measure at least at two different flow rates(or breathing rates) and plot the values obtained on the standard curve. This would then give information as to a) the value of nasal resistance as compared to an established standard and b) the tendency of the curve (i.e., the slope). The latter would indicate the presence or the absence of a "reserve capacity" with regard to air passage through the nose.

With this slight addition, this writer feels both methods could be developed into useful tools. The method of Seebohm and Hamilton seems to have some advantage in the simplicity of its procedure.

SUMMARY

Measurement of nasal flow resistance has been evaluated because of a recent revival of interest in this subject. It has been shown that the assessment of nasopharyngeal pressure and nasal flow rate in a single measurement is not sufficient since this function is linear only over a limited range. Nonlinearity is introduced as soon as the nasal airflow starts eddying. Although laminary at low breathing rates and in normal noses, the air flow is at the verge of eddying which

starts at very slight provocation (accelerated breathing, narrowing of the nose, etc.). Present methods of measurement can be improved by taking the nonlinearity of the pressure to flow relation into account.

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LXXIV

A METHOD FOR HUMIDIFYING INSPIRED AIR IN POSTTRACHEOTOMY CARE

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All over the world the number of tracheotomies has increased during the last decade owing to extended indications. Attention has more and more tended to be focused on the postoperative care of these cases since the majority of complications, above all pulmonary ones, appear in the postoperative stage (e.g., tracheobronchitis, atelectases, pneumonias, etc.). Infection and secretional occlusion of the air passage are favored by several factors, e.g.:

1. The loss of filtering out of airborne particles in the nasal cavity.

2. Excess secretion and aspiration.

3. Frequent non-aseptic suctions of the tracheobronchial tree.

4. Insufficient warming and humidification of inspired air, injuring and drying the respiratory epithelium, resulting in impaired cilial activity[1,2] and causing viscous secretion and crusts.

The authors of this paper have devised a method for raising the humidity content of the inspired air to a more physiologic level than that found when air of ordinary room temperature and humidity is inhaled directly through the tracheal stoma. Attempts have earlier been made to solve the problem of humidifying inhaled air in tracheotomized patients according to the following two principles:

1. External humidification of the air.

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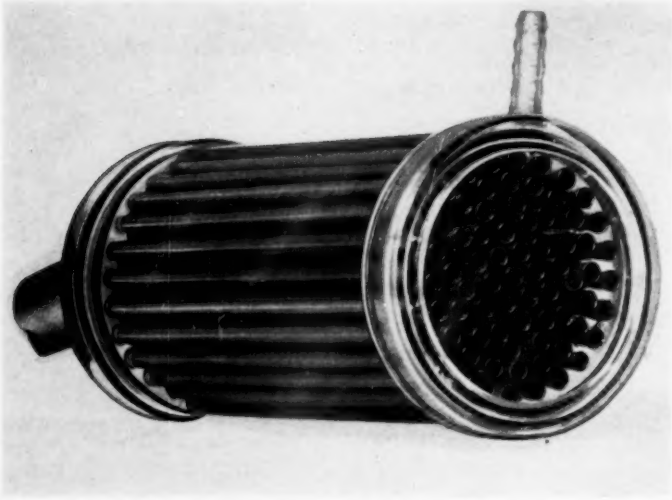

Fig. 1.—The heat-and-moisture exchanger consisting of stainless steel tubes in a plexiglass cylinder.

This can be done by means of hot steam, mechanical evaporization (cold steam), or intratracheal injections of saline or other solutions.

2. Internal humidification of the air. By means of special arrangements, part of the humidity of the expired air is conserved by condensation and transferred to the inspired air by evaporation. According to this principle a condensation cylinder for nasal application is described by Proetz.[3]

It is common to all methods based on the two above-mentioned principles that until now, no reliable determinations of their air-conditioning capacity have been made.

The present authors, preferring a method based on the condensation principle, have constructed a heat-and-moisture-exchanger (HME) designed by one of us (Allander). This is a tubing system in which the inspired air recaptures part of the heat and humidity from the expired air. In order to determine the efficiency of such a system we have used a method described by Ingelstedt[4] for continuous, simultaneous recording of the changing temperature and relative

humidity of the air passing through the apparatus. The method involves the use of a thermo-electric psychrometer.

It is known from earlier investigations[4] that the expired air of a normal individual has an absolute humidity of 42 g/m^3 when passing through the larynx and that the inspired air at the same level contains 35 g/m^3. After tracheotomy we have found the absolute humidity to be about 40 g/m^3 when the expired air passes the tracheal stoma. The inspired air, however, on the same measuring point, holds only 7-8 g/m^3 (room air at 24° C - 25° C and a relative humidity of 30 - 35 per cent). In view of these values, there are great possibilities of using any form of a HME for recapturing at least a certain amount of the water in the expired air.

In the construction of a HME for clinical use, the following demands must be satisfied:

1. The largest possible inner surface, on which the humidity of the expired air can condense and from which the inspired air is moistened.

2. The smallest possible dead space.

3. The exchanger must not increase the resistance to the air flow beyond physiologic limits.

4. The exchanger must be easy to apply and to handle, and the patient must not be exposed to any danger.

The theoretical calculations for a HME of the kind described here are as follows:

The degree of dry heat recovering efficiency (η) of the HME is obtained from the following equation (at small intervals of time):

$$\eta = \frac{1}{1 + \frac{2G_g c_v}{\alpha F}}$$

in which

α = the heat transfer coefficient between the air and the inner surface of the stainless tubes.

F = the total inner heating surface of the HME

G_g = the air volume per time unit.

c_v = the specific heat of the air

In all tests performed, the air flow through the HME's was 19.2 litres/min (corresponding to 16 respirations/min; tidal volume 600 ml). This gives $G_g = 1.35$ kg/h. The specific heat of the air is 0.24 kcal/kg °C. The inner heating surface is $59 \cdot L \cdot 10^{-4}$ m^2, where L is the length of the HME in cm. The heat transfer coefficient (α) may be calculated from a ratio deduced by Sieder and Tate[5] and valid for laminar air flow in tubes:

$$\frac{\alpha D}{\lambda} = 1.86 \cdot \left(\frac{vD}{v} \cdot \frac{v}{a} \cdot \frac{D}{L} \right)^{1/3}$$

to

$$\alpha = 48.6 \cdot L^{-1/3} \text{ kcal/m}^2\text{h °C (L in cm)}$$

These calculations yield the degree of efficiency:

$$\eta = \frac{1}{1 + \frac{2.21}{L^{2/3}}}$$

In Table I the computed efficiency degrees are obtained for some different magnitudes of L. The column to the right in the table denotes the degree of recaptured water obtained during the experiments with saturated air.

According to these theoretical calculations a HME was constructed, the details of which appear in Figure 1.

The expired and inspired air is allowed to pass through a tube system of stainless steel, consisting of 75 tubes with an inner diameter of 2.5 mm and an outer one of 3 mm. The tubes are enclosed in a plexiglass cylinder. Other details of the equipment are a lid of the same material and a flexible tube connected to the tracheal cannula. If necessary for practical use the distal end of the exchanger may be provided with a ring-shaped additional piece, to which oxygen may be conducted and distributed in front of the distal end through small apertures placed around the periphery of the additional piece.

Comparative experiments have been made with a series of HME's of varying lengths (2½, 5, 10, 20 cm). The data valid for their condensation surface and dead space appear in Table II (the connect-

TABLE I

CALCULATED AND MEASURED DEGREES OF RECOVERING EFFICIENCY IN RELATION TO DIFFERENT LENGTHS OF HME's

LENGTH IN CM L	CALCULATED DEGREE OF HEAT RECOVERING EFFICIENCY	MEASURED DEGREE OF MOISTURE RECOVERING EFFICIENCY
2.5	0.46	0.29
5	0.60	0.55
10	0.68	0.61
20	0.77	0.65

TABLE II

COMPUTATION OF THE RESPECTIVE VALUES OF THE INNER SURFACE, DEAD SPACE, AND RESISTANCE TO STEADY FLOW OF HME's OF DIFFERENT LENGTHS

LENGTH OF THE HME IN CM	INNER SURFACE IN CM^2	DEAD SPACE IN CM^3	RESISTANCE TO STEADY FLOW (100 litres/min in mm H_2O)
2.5	148	9	5
5	295	18	5
10	590	36	6
20	1180	72	8

ing tube is not included in the calculations). The resistance to steady flow through the tube system in mm H_2O is determined at a rate of 100 litres/min.

In order to obtain an objective estimation of the different HME's it is imperative to provide for a uniform ventilation and constant temperature and humidity of expired and inspired air in all experiments. This has been achieved with the aid of an experimental device, similar to a respirator and consisting of two electric fans. The air-flow through these fans is regulated by two electromagnetic valves which open and shut alternately (Fig. 2).

During expiration the air passes through a saturator, regulated by a thermostat and containing distilled water at a constant

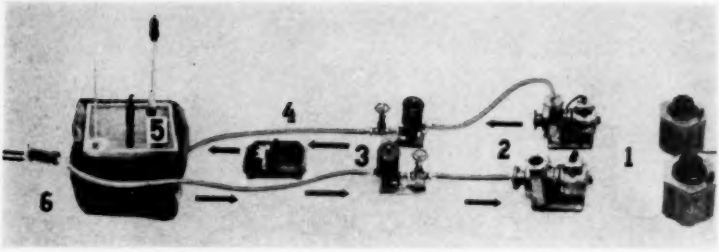

Fig. 2.—The experimental device. 1. Variable autotransformers. 2. Electric fans. 3. Electro-magnetic valves. 4. Magnetic valve-changer. 5. Saturator. 6. Heat-and-moisture exchanger.

temperature of 37° C. The inspired air has a temperature of 24° C to 25° C and a relative humidity of 30 to 35 per cent. In all experiments referred to below the respirator system worked at a constant frequency of 16 respirations/min and constant tidal volumes of 600 ml. The volumes have been carefully determined in a gas meter and are equal at expiration and inspiration.

The determination of the temperature and humidity of the expired and inspired air has then been made with the above-mentioned micropsychrometer immediately proximally and distally to the HME. The thermo-element wires of the latter have a diameter of only 0.03 mm and they have been soldered end-to-end so that the soldering junctions do not exceed the diameter of the wire. One of the thermo-elements is provided with a wetting wick in such a way that the total diameter of metal wire plus wick does not exceed 0.1 mm.

With the aid of this instrument it is possible to obtain a practically simultaneous recording of the variations in the temperature and relative humidity of the air passing the measuring points. The cold junction has been immersed in ice at a temperature of 0.0° C. The potentials which arise in the hot junctions have been converted to a 50 c/s alternating current by means of Brown converters. The output voltage has been recorded with a direct 2-channel ECG apparatus (Mingograph, Type 230, Elema Ltd., Stockholm). In order to increase the sensitivity within a small range of temperature, bucking voltages were inserted into every thermoelectric circuit in such a way that in all recordings the zero line was shifted to 25.0° C (See Fig. 3).

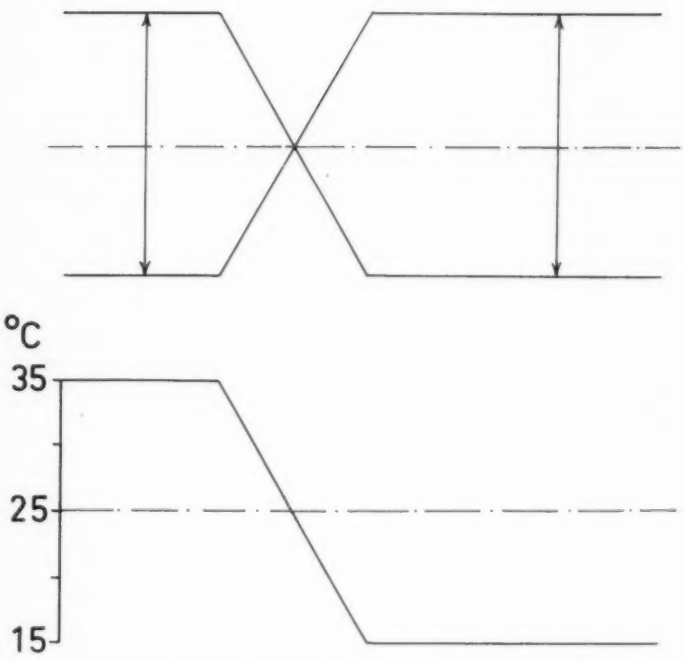

Fig. 3.—Principle of temperature recording. Above: The appearance of the recorded temperature curve. Below: The appearance of the computed curve. (Thus a recorded temperature curve at 15° C has the same appearance as a curve at 35° C.)

RESULTS

The experimental recordings are illustrated in Figure 4. The temperature of the air is calculated from the dry thermo-element (DT) recordings (solid line). The relative humidity is calculated from the dry and wet thermo-element (WT) recordings (broken line) and the values are obtained from special psychrometric tables.

Expiration. When entering the HME from the saturator, the air has a temperature of about 36° C to 37° C and a relative humidity of 100 per cent in all four model experiments. When this air passes the four HME's, whose tubing systems have different lengths, the air is more effectively cooled with increasing length, as appears in the curves of the upper half of Figure 4. Thus in the 2½ cm HME

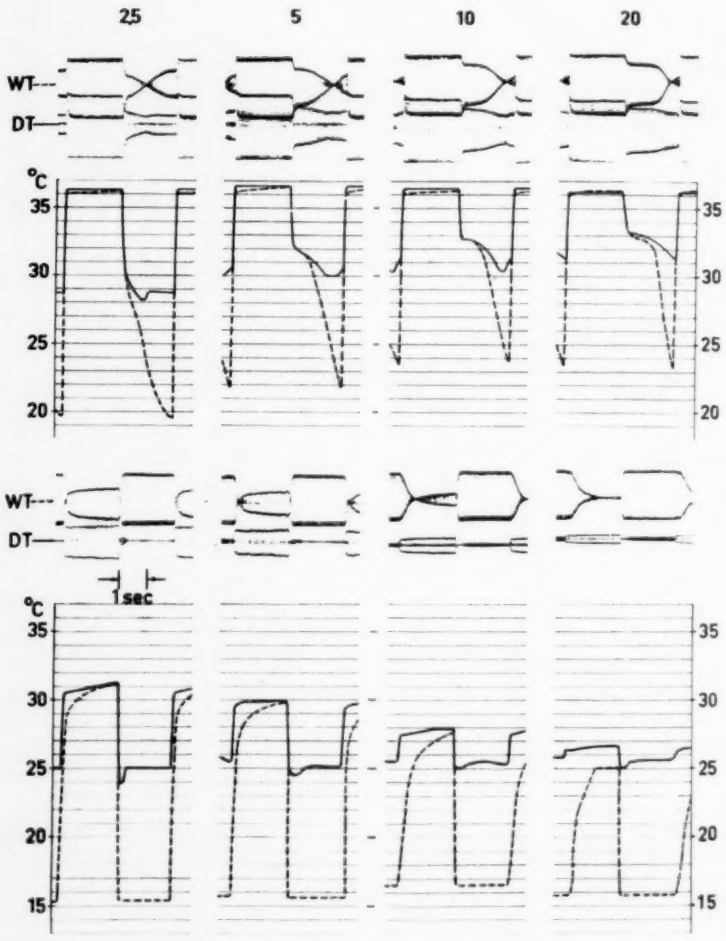

Fig. 4.—Experimental recordings of the dry (DT) and wet (WT) thermo-elements in testing the 2½, 5, 10 and 20 cm HME's and the corresponding calculations for the temperature and relative humidity.

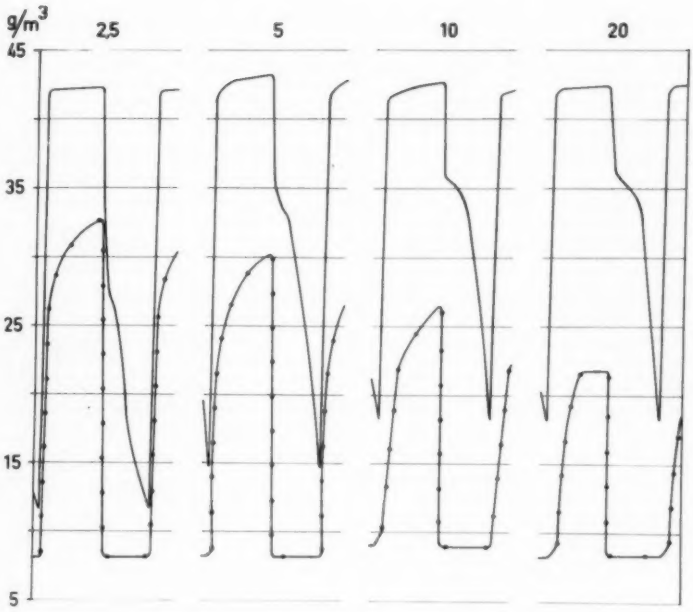

Fig. 5.—Calculations of the absolute humidity in the experiments with the four HME's as plotted from Figure 4.

the expired air has a temperature of 31° C, whereas the temperature is 25° C when leaving the 20 cm HME. The relative humidity of the expired air is 85 to 100 per cent towards the end of the expiratory phases, as appears from the curves in the lower half of Figure 4 (from difference DT – WT). With increasing length of the HME it is found, furthermore, that an increasing air volume at the beginning of the expiratory phase has a lower relative humidity.

Inspiration. In all model experiments, the room air has a temperature of about 25° C and a relative humidity of 30 to 35 per cent before entering the HME (see lower half of Figure 4). After the air has passed through the HME it is warmed between 3° C and 7° C. The longer the HME, the more effective is the heating of the air (upper half of Figure 4). The relative humidity of this air, calculated at the end of the inspiratory phase, increases only from about 40 per cent to about 55 per cent with increasing length of the HME. It is noteworthy, however, that in the shorter systems the major

TABLE III

MEAN TEMPERATURES AND MEAN ABSOLUTE HUMIDITIES AT BOTH RESPIRATORY PHASES AND DIFFERENT LENGTHS OF HME's

Length of the HME in cm	2.5		5		10		20	
	°C	g/m³	°C	g/m³	°C	g/m³	°C	g/m³
Expired air before entering the HME	36.2	42.0	36.6	42.8	36.4	42.2	36.2	42.0
Inspired air before entering the HME	25.0	8.1	25.0	8.1	25.2	9.0	25.6	8.2
Expired air after leaving the HME	31.0	31.3	30.0	26.0	27.9	21.6	26.5	19.1
Inspired air after leaving the HME	27.8	17.5	30.8	25.8	31.4	29.0	32.5	30.2

part of the inspiratory volume has a low relative humidity, but with increasing length of the HME the less conditioned air portion decreases (calculated from the beginning of the inspiratory phase as seen in the upper half of Figure 4).

The changes in absolute humidity, plotted from Figure 4, are demonstrated in Figure 5. The solid line in this figure shows the changes of the absolute humidity of the expired air when entering the HME (peak turned upwards), and the inspired air when it has passed the HME (peak turned downwards). In like manner, the dotted line is an expression of the absolute humidity value of the expired air after leaving the HME and that of the inspired air before entering the HME. As appears from the figure, the absolute humidity of the expired air is constant at 42 g/m³ before entering the HME. After the air has left the apparatus, decreasing amounts of absolute humidity are obtained with increasing length of the HME. During the inspiratory phase the absolute humidity increases with the increasing length of the HME, but is comparatively low in all experiments at the end of the inspiratory phase.

Both during expiration and inspiration the flow velocity is comparatively constant. As the psychrometer is capable of a practically simultaneous recording, it is possible to calculate the mean temperature and the mean absolute humidity of the whole air volume for each particular breath. This calculation has been made by integrating the recorded temperature curves. The following values have been obtained from these calculations (see Table III).

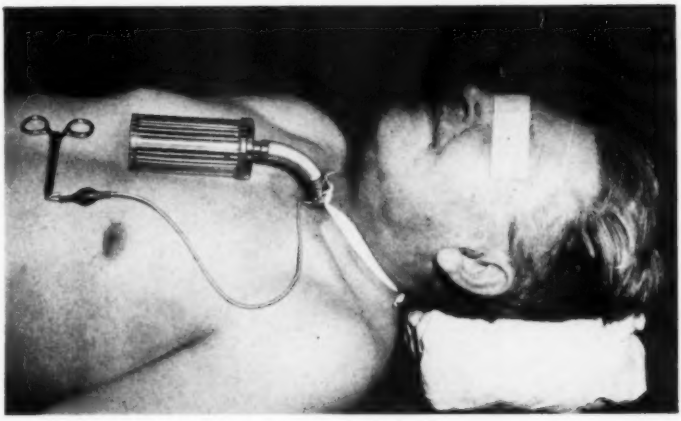

Fig. 6.—The HME connected to the tracheal tube of a laryngectomized patient.

COMMENT

It appears from these experiments that it has been possible, with the aid of a heat-and-moisture exchanger (HME) of the type described above, to raise the temperature and humidity of the inspired air considerably. As is apparent from the experiments, however, the relative humidity is low at the end of the inspiratory phase even when a 20 cm long HME is used. It could be observed in the experiments that the visible condensation zone which appears in the HME during expiration, disappears during the subsequent inspiratory phase. The less well conditioned air at the end of the inspiration, when the longer HME's are used, can hardly influence the humidity and temperature of the air reaching the alveoli, since a major part of this end portion remains in the dead space. It is further found that the mean absolute humidity reaches the 29 to 30 g/m^3 level during the inspiration through the 10 cm and 20 cm HME's. When the inspired air passes through the larynx during nasal breathing in a healthy non-tracheotomized resting patient, the mean absolute humidity is about 35 g/m^3. Using the described HME of 10 cm and 20 cm, it is not possible to reach ideal values. As the level of the absolute humidity of the room air, however, is only 7 to 8 g/m^3, the increase to 29 to 30 g/m^3 must be regarded as considerable and is satisfactory in view of the simplicity of the construction.

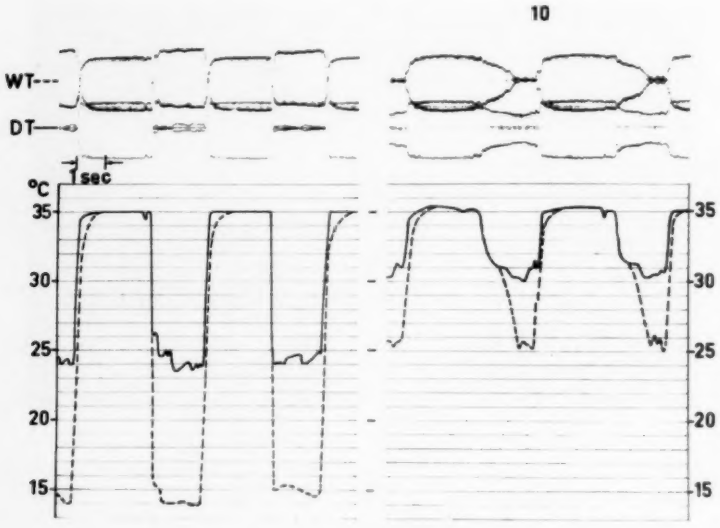

Fig. 7.—Recordings of the dry (DT) and wet (WT) thermo-elements from a laryngectomized patient. To the left without and to the right provided with a 10 cm HME. Below the calculations for the temperature and relative humidity.

The efficiency of the HME is the ratio of the amount of water vapor of the inspired air obtained after passing the HME to the total amount of water vapor condensed from expired air. The values from these calculations are obtained from Table I. From this it follows that the efficiency of the 5 cm to the 20 cm HME's is ranged from 55 to 65 per cent. The 2.5 cm HME has a much lower efficiency.

The 10 cm HME, which has been found to best satisfy physiologic requirements (air conditioning capacity, air flow resistance, dead space, etc.) is now being tested for practical use, and thus far the results have been encouraging. The apparatus seems to be best suited for tracheotomized patients with viscous and inspissated secretions. For patients with high fever it is favorable too, because the rise in body temperature results in a greater loss of water from the respiratory tract. The same principle for a HME may also quite well be used in respirator treatment, since in this case air resistance and dead space of the HME are small.

In Figure 6 an example of the practical use of the HME is demonstrated. A laryngectomized patient is provided with a 10 cm long HME, connected to the tracheotomy tube provided with an inflated cuff. The recordings from this patient are seen in Figure 7. To the left, recordings are made in the tracheal stoma without a HME and to the right in the flexible tubing which connects the HME with the tracheal tube.

After passing the tracheal stoma, the expired air has a temperature of 35.5° C and a relative humidity of 100 per cent (i.e., absolute humidity of 40 g/m^3). The inspired air without a HME has a temperature of 24° C to 25° C and a relative humidity of about 35 per cent (i.e., absolute humidity of 7 g/m^3). After application of the 10 cm HME for only half an hour the minimum temperature of the inspired air is found to have risen to 30° C to 31° when leaving the HME, and the relative humidity has increased to 60 to 70 per cent as a minimum. Thus the absolute humidity of the inspired air increases three to four times after only half an hour's use of the HME, as compared with experiments made without it.

SUMMARY

The authors describe a method for humidifying inspired air in tracheotomized patients. A heat-and-moisture exchanger is constructed, consisting of a metal tubing system in which moisture deposited by condensation during expiration is recaptured by the subsequent inspiration. The air conditioning capacity of such tubing systems of different lengths is determined in model experiments and on patients. From the experiences acquired in these experiments, the authors conclude that an exchanger with a dead space of 36 ml and an inner metal surface of about 600 cm^2 is preferable in the case of adults.

The moisture recovery efficiency of the exchanger is determined at 61 per cent. This gives an increasing absolute humidity of the inspired air from 7 to 29 g/m^3 after passing through the tubing system. In other words the absolute humidity of the inspired air is only about 20 per cent below that of inspired air at the same level during normal nasal inspiration (absolute humidity 35 g/m^3).

UNIVERSITY OF LUND

Mr. Walther Lütke gave valuable assistance in manufacturing the HME's.

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LXXV

MALIGNANT LESIONS OF THE NASOPHARYNX

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Always a challenging problem, both from the diagnostic and therapeutic standpoint, malignant lesions of the nasopharynx are perhaps the most commonly misdiagnosed, most poorly understood, and most pessimistically regarded of all tumors of the upper part of the respiratory tract. Opinions on the salvageability of patients with such tumors range from the more hopeless outlook of Eggston,[1] who stated: "These tumors are ray sensitive for awhile, but all [patients] succumb in from one to three years," to the more optimistic reports of Lenz,[2] Nielsen,[3] Martin and Blady,[4] and Godtfredsen,[5] who have achieved five-year survival rates of 25 per cent or thereabouts. The nasopharynx is not a common site for malignant neoplasms. Godtfredsen estimated that such lesions constitute approximately 0.3 to 0.4 per cent of all malignant lesions of human beings and about 0.8 per cent of the malignant lesions seen in radiologic clinics. Simmons and Ariel[6] stated that they constituted about 0.7 per cent of all malignant lesions of man and 11.5 per cent of all intraoral carcinomas. Martin and Blady[4] gave a more generous estimate of 2.0 per cent of all malignant growths as contrasted to the more common carcinoma of the tongue which is responsible for 7 per cent, and of the tonsil for 3 per cent of the malignant lesions. Godtfredsen maintained that a real increase in the incidence of the disease has occurred in recent years over and above the increase expected from improved diagnostic facilities and increased awareness. In this report we shall review a

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Read at the meeting of the Minnesota State Radiological Society, Minneapolis, Minnesota, March 1, 1958.

From the Sections of Therapeutic Radiology, Plastic Surgery and Surgical Pathology of the Mayo Foundation, Rochester, Minnesota, a part of the Graduate School of the University of Minnesota.

series of 88 cases of primary malignant growths of the nasopharynx seen at the Mayo Clinic in the five years, 1945 through 1949.

AGE AND SEX INCIDENCE

Seventy of our patients were male and 18 female. This ratio of about four to one for males to females is in accord with the male predominance in most reported series. It is of interest to note that Russell[7] found a statistically significant better survival rate in females with this disease. Simmons and Ariel,[6] reporting on an all-male series from a Veterans Administration Hospital, have a low five-year survival of 9.8 per cent of 78 men, and it is interesting to speculate how much of an effect the sex incidence may have had on their results. The age at onset of the disease has varied in all reported series from the very young to the very old, with a peak incidence, as might be expected, in the fifth and sixth decades of life. The youngest patient in our series was five years, the oldest 78 years. There was one patient in the first decade, five in the second, seven in the third, 12 in the fourth, 26 in the fifth, 25 in the sixth, ten in the seventh, and two in the eighth. The average age was 45.5 years. Simmons and Ariel stated that malignant lesions occur in the nasopharynx of children and adults less than 30 years of age more often than in any other part of the upper respiratory or alimentary tracts. In our series, there were 25 patients (28 per cent) less than 40 years of age.

PATHOLOGIC ASPECTS

There is probably no other single regional group of malignant lesions of the upper part of the respiratory system with less agreement in the world literature with regard to the correct and proper pathologic classification. It is not within the scope of this paper to attempt to define the pathologic boundaries between the various subgroupings of nasopharyngeal malignant lesions. It is, however, well to bear in mind, as Eggston has previously emphasized, that many of these tumors are so poorly differentiated and classification is so poorly agreed on that comparative morbidity statistics are unreliable. This was most graphically illustrated by Godtfredsen in his comprehensive review of available literature. He pointed out that the numerous authors whose reports were reviewed, listed the incidence of carcinoma as 8 to 92 per cent with an average of 55.6 per cent, while the frequency of squamous cell epithelioma as a subgrouping of the carcinomas was given as from 76.5 to 100 per cent. The undifferentiated

TABLE I

PERCENTAGE INCIDENCE OF THE VARIOUS MALIGNANT LESIONS OF THE NASOPHARYNX IN NINE SERIES REPORTED IN THE LITERATURE

	SQUAMOUS CELL EPITHELIOMA	OTHER CARCINOMA	LYMPHO-EPITHELIOMA	TRANSITIONAL CELL CARCINOMA	LYMPHOSARCOMA	OTHER SARCOMAS	OTHERS
Present Mayo Clinic	19		67		5		9
Godtfredsen	39.3	15.9	10.6	2.5	3.9	24.9	2.8
Nielsen	26	15.5	28.5		9	17	4
Graham and Meyer	24			58.5	3.5		13.5
New	67.8				15.9		6.3
Martin	6		16	48	12.5		17.5
Eberhard and Leaming	40		10		40		10
Lenz	43		32		19		6
Simmons and Ariel	34.7	9.3		30.7			

carcinomas are apparently an even more perplexing problem; the frequency of lympho-epitheliomas and transitional cell carcinomas as a combined group varied from 0 to 100 per cent. Most authors hold the view that separation of lympho-epithelioma from transitional cell carcinoma rests on such tenuous grounds that the separation is not valid. Godtfredsen said that of the many authors whose articles he reviewed only Ewing and Schinz and Zuppinger maintained that it is possible to separate the two. Interestingly enough Ewing reported an incidence of transitional cell carcinoma of 79.2 per cent out of the total of both, whereas Schinz and Zuppinger reported an incidence of lympho-epithelioma of 78.8 per cent out of the total of both. The confusion continues with the classification of lymphosarcoma. Here the variation in the world literature ranges from an incidence of 5.1 to 53.4 per cent.

Some of the extreme variability in the pathologic classification of nasopharyngeal malignant lesions is indicated in Table I.

In our study malignant lesions of the nasopharynx are subdivided into 1) squamous cell carcinoma which includes all recognizable de-

grees of squamous differentiation, 2) lympho-epithelioma, and 3) lymphosarcoma. Under the heading "lympho-epithelioma" are included all undifferentiated carcinomas whether lympho-epithelioma or transitional cell type. Although we do not deny the possibility of a subdivision within this group, it was thought best to group all such tumors in a single category until clear-cut definitions of subtypes can be agreed on. The nine per cent of our series labeled as "others" in Table I consists of three cases of small cell carcinoma, one case of adenoid cystic carcinoma or cylindroma, one case in which biopsy was performed elsewhere and the lesion was merely called malignant, two cases in which a clinical diagnosis only was made, but in which the eventual outcome left little doubt as to the malignancy of the process, and one case of adamantinoma. The inclusion of this last case in a series of nasopharyngeal malignant lesions may be open to question, but since it presented as, and was treated primarily like, a nasopharyngeal malignant lesion, it was included. Its exclusion would not change our statistics significantly.

Godtfredsen found too that sarcomas occur twice as frequently as carcinomas among patients less than 40 years of age, and our figures would substantiate this impression. Of 25 patients in our series less than 40 years of age, 72 per cent had sarcoma, 20 per cent squamous cell carcinoma, and the rest miscellaneous lesions.

MORPHOLOGY AND LOCATION

Without doubt the nasopharyngeal malignant neoplasm is one of the most commonly misdiagnosed neoplasms of the head and neck. Doubtless this is due to the relative inaccessibility of the nasopharynx and the unfamiliarity of many medical men with the nasopharyngeal mirror. Thus, it is much commoner for the patient afflicted with a malignant lesion of the nasopharynx to seek medical attention because of secondary extension to the regional nodes of the neck or at the base of the skull or because of involvement of the base of the skull and neighboring cranial nerves. Of our 88 cases only one was asymptomatic and in that one the nasopharyngeal lesion was picked up in the course of an examination for unrelated complaints.

Some authors have tried to correlate the morphologic aspects with the pathologic appearance of the primary tumor and have stressed that epitheliomas tend to present as smaller, often ulcerating well-demarcated lesions as contrasted to the sarcomas which more often present as larger bulkier tumors with less tendency to ulcerate and a greater tendency to infiltrate submucosally beyond the ap-

parent limits of the tumor. We have considered that such correlation is of little clinical value and as with most other malignant lesions, attention to the form of the primary lesion is at best unrewarding.

From the morphologic standpoint alone, lesions such as juvenile nasopharyngeal fibromas, chordomas, craniopharyngiomas, plasmacytomas and, to a less extent, teratomas, hemangiomas, lymphangiomas, posterior choanal polyps, and tuberculous retropharyngeal lymph nodes, and rarely pituitary tumors or the osteochondrofibroangiomatous tumors may resemble primary malignant lesions of the nasopharynx so closely that any attempt to discriminate on morphologic grounds alone is worthless. The surest and only method of differentiation, as with all malignant lesions, lies with biopsy.

Many authors, likewise, have tried to correlate the location of the primary nasopharyngeal malignant lesion with the eventual clinical course, in particular with regard to the mode of dissemination or direction of metastasis.

In 47 (53 per cent) of our 88 cases the exact point of origin could not be determined accurately because in 21 patients the bulk or mass of the lesion was so large that it obscured the point of origin, and in 26 the clinical description of the lesion was lacking in some detail. Simmons and Ariel reported that 40 per cent of their lesions were of indefinite or unascertained origin, an experience in common with most reported series. In our cases in which the exact origin of the neoplasm could be ascertained, 29 per cent were found to arise from the immediate vicinity of the fossa of Rosenmüller, 46 per cent arose directly from the vault of the nasopharynx, 10 per cent from the anterior wall immediately above the posterior choana, and 15 per cent from the posterior wall.

Lenz has maintained that lesions arising in the vault and from the region of the fossa of Rosenmüller have a somewhat greater tendency to invade the base of the skull and involve regional cranial nerves; this is a most logical assumption considering the proximity of these two regions to the foramen lacerum, the most common avenue of extension cranialward. Our figures, however, indicate just as great a tendency on the part of posterior and lateral wall tumors to infiltrate superiorly as those arising from the vault and fossa of Rosenmüller (Table II).

If any conclusion can be drawn from these figures, it is that posterior and lateral wall lesions are the most unfavorable as regards

TABLE II

INVASIVE TENDENCIES OF MALIGNANT LESIONS AT VARIOUS SITES IN THE NASOPHARYNX

SITE OF LESION	PATIENTS	NODES INVOLVED, PER CENT	BASE OF SKULL INVADED, PER CENT
Fossa of Rosenmüller	12	83	8
Vault	19	47	53
Anterior wall	4	75	25
Posterior and lateral wall	6	83	100
Extensive	21	62	57
Indeterminate	26	70	42

dissemination in either direction. Yet because of the small number involved, we hesitate to attach much significance to this broad generalization.

DISSEMINATION

Since the secondary or metastatic manifestations of the disease commonly bring the condition to light, it is well to consider briefly the various avenues of dissemination from the nasopharynx. Dissemination laterally and posteriorly is probably the most common. This route, which Ackerman and del Regato[12] referred to as the "retroparotidean" route, entails invasion of the retromandibular region with possible subsequent involvement of the palatal muscles, the third branch of the V cranial nerve, and in close apposition to these, the IX, X, XI, and XII cranial nerves along with the upper portion of the sympathetic trunk. Hence several or all of these nerves may be involved by a small, clinically undetectable posterior extension along the base of the skull in the region of the jugular foramen and hypoglossal canal, or by contiguous pressure from metastatically involved nodes in this region. As frequent as the nerve complications are, they are overshadowed by the frequency of involvement of the nodes in this region. The retropharyngeal lymph nodes because of their immediate proximity to the nasopharynx are the earliest and most frequently involved of the regional nodes, yet because of their inaccessibility this involvement almost never is recognized prior to involvement of the more superficial secondary chain, the deep cervical

lymph nodes. Of these, by far the most commonly involved is the superior lateral cervical node just beneath the mastoid process. From there, of course, any or all of the descending cervical nodes may be involved down to and beyond the thoracic inlet.

Probably the most serious and second most frequent route of dissemination is superiorly through the base of the skull into the floor of the middle fossa. The foramen lacerum, barely a centimeter from the juncture of the lateral wall and vault of the nasopharynx, is by far the most common point of entry, with or without invasion of the surrounding sphenoid, petrosa, or occiput. Invasion via this pathway which Ackerman and del Regato referred to as the "petrosphenoid" route entails early and readily recognizable involvement and destruction of the basilar cranial nerves in almost direct proportion to their proximity to the foramen lacerum and immediately adjoining cavernous sinus. Thus the VI, III, and IV cranial nerves, and the ophthalmic and maxillary branches of the V cranial nerve along with the sympathetic carotid plexus may be involved jointly by a small lesion invading the cavernous sinus. Various types of ophthalmoplegia with or without involvement of the V cranial nerve are among the earliest manifestations of intracranial extension of malignant lesions of the nasopharynx. Only in the more advanced case when extension forward along the anterior floor of the middle fossa has occurred is involvement of the optic nerves, the orbit or the anterior fossa recognized. Posterior extension into the posterior fossa is much rarer, although possible, together with involvement of the VII and VIII cranial nerves resulting in nerve as opposed to conduction deafness, disturbed vestibular function and peripheral facial paralysis. The dura mater is resistant to penetration although late in the course of the disease superior invasion may result with destruction of the mesencephalon, cerebral peduncles, optic tracts, and temporal lobes.

Less common routes of dissemination from the primary lesion in the nasopharynx go anteriorly to involve the nasal cavity, ethmoid sinuses, maxillary antrum and less commonly the orbit via the superior orbital fissure, the anterior cranial fossa via the lamina cribrosa, and the pterygopalatine and infratemporal fossas; inferiorly with mucosal spread to involve the fauces, palate, lateral hypopharyngeal wall and base of the tongue; and much less commonly posteriorly where extension is less readily achieved due to the dense facial planes attached to the base of the skull. Penetration, however, does occur in an occasional case with extension into the cervical portion of the spinal canal and posterior cranial fossa.

TABLE III

PRESENTING SYMPTOMS

	CASES	PER CENT
Pain of head or neck	43	49
Cervical adenopathy	41	47
Loss of hearing	30	34
Nasal obstruction	25	28
Ear block or tinnitus	18	20
Nasal or oral bleeding	18	20
Diplopia	15	17
Blurred vision	4	5
Ear pain	11	12
Dysphagia	10	11
Facial paresthesia	8	9
Paralysis of cranial nerve	8	9
Sore throat	8	9
Visible tumor below the palate	5	6
Weakness and fatigue	4	5
Loss of weight	3	4
Peripheral arthritic pain	3	4
Trismus	2	2
Sinusitis, anosmia, vertigo, orbital protrusion, ataxia, nervousness	1 each	1 each
Routine investigation for other complaints	1	1

Presenting symptoms in our 88 cases give a fairly reliable index of the frequency and mode of extension of the primary nasopharyngeal neoplasm (Table III).

Of the 88 patients studied, only 20 (23 per cent) had evidence of localized disease, that is, no involvement of a cranial nerve or other evidence of invasion of the base of the skull, metastatic invasion of the cervical nodes or evidenec of systemic dissemination. Forty-one (47 per cent) had palpable cervical nodes when first seen, 11 (12 per cent) had evidence of cranial nerve involvement or roentgenologic demonstration of destruction or invasion of the floor of the middle fossa only, and 14 (16 per cent) had both cranial nerve involvement or destruction of the base of the middle fossa and metastatic cervical adenopathy. Two had clear-cut evidence of distant dissemination at the time of initial examination, one with metastatic invasion of the

anterior chest wall, the other with systemic dissemination to lungs, liver, and abdominal nodes.

METASTATIC LESIONS OF THE CERVICAL NODES AND RELATED HISTOPATHOLOGY

The incidence of metastatic involvement of the cervical nodes as one of the initial or presenting complaints varies widely in the literature from a low of 20 per cent reported by Cappell[13] to the 80 per cent reported by Salinger and Pearlman.[14] Our own figures indicate that 47 per cent of our 88 patients had lesions in the cervical nodes at the time of initial examination and that 63 per cent had metastatic cervical adenopathy at some stage in their disease.

A review of the lesions in our cases in which the cervical nodes were involved tends to substantiate the general impression that sarcomas and related neoplasms have a greater tendency to disseminate to regional nodes than do the carcinomas (Table IV).

TABLE IV

INCIDENCE OF METASTATIC INVASION OF CERVICAL NODES AND INVOLVEMENT OF CRANIAL NERVES OR BASE OF THE SKULL

PATHOLOGY	INVOLVEMENT, PER CENT OF CASES	
	CERVICAL NODES	CRANIAL NERVES OR BASE OF SKULL
Lymphosarcoma	75	25
Lympho-epithelioma	73	27
Squamous cell epithelioma	35	35
Small cell carcinoma	66	33

BASE OF THE SKULL AND CRANIAL NERVE INVOLVEMENT AND ITS RELATED HISTOPATHOLOGY

A total of 37 cases (42 per cent) out of our series of 88 had involvement of the cranial nerves at some stage in their disease. At the time of initial examination 24 (27 per cent) showed evidence of cranial nerve involvement or paresis and an additional 13 (15 per cent) showed such evidence at a later date.

TABLE V

FREQUENCY OF INVOLVEMENT OF VARIOUS CRANIAL NERVES IN 37 CASES

CRANIAL NERVE	INVOLVEMENT, CASES		
	INITIAL	LATER	TOTAL
2	1	0	1
3	3	2	5
4	3	1	4
5	8	2	10
6	20	9	29
7	4	2	6
9	6	4	10
10	5	3	8
11	1	2	3
12	6	3	9

The frequency with which the various cranial nerves were involved can be seen from Table V.

The V and VI cranial nerves are most frequently involved when the primary nasopharyngeal neoplasm extends cranialward through the base of the skull while the IX, X and XII cranial nerves are the ones most commonly affected when the disease extends laterally and posteriorly into the retropharyngeal region and along the floor of the posterior fossa.

Roentgenographic evidence of invasion or destruction of the floor of the middle fossa is a much less common although a concomitant manifestation of extension cranialward. In seven cases (8 per cent) there was roentgenographic evidence of destruction either in the region of the foramen lacerum or the sphenoid at the time of initial examination, while in an additional four cases (5 per cent) such invasion was demonstrated later. We are sure this figure is unduly low since less than half of the total number of patients had roentgenograms of the base of the skull, a procedure which today is considered essential in all cases of nasopharyngeal malignant lesions. Lenz reported that half of his patients who had roentgenograms of the base of the skull presented roentgenographic evidence of bone invasion.

Martin[10] reported that approximately a third of all his patients showed roentgenographic evidence of destruction of bone and Needles[15] reported an over-all incidence of such destruction in 63 per cent of his cases. Godtfredsen quoted Jonsson as stating that approximately a third of his patients had malignant invasion of the floor of the middle fossa while Godtfredsen himself noted an incidence of 29 per cent with invasion being five times more frequent in patients with neurologic symptoms than in those without. The actual site of invasion in almost all reported series is in the immediate vicinity of the foramen lacerum. Lenz has attempted to define the actual point of destruction a bit more closely and listed the following in descending order of frequency: the body of the sphenoid, the greater wings, the petrosa, and the occipital bone.

From Table IV, it can be seen that all of the pathologic subgroups in our series tended to invade superiorly with about equal facility, the tendency being slightly greater in the squamous cell epithelioma group. Lenz expressed the view that squamous cell epithelioma has a distinctly greater tendency than the other lesions to invade the base of the skull early, lympho-epithelioma has somewhat less tendency than the squamous cell epithelioma, and lymphosarcoma rarely invades superiorly. Godtfredsen stated that although the epitheliomas have a slightly greater tendency than sarcomas to invade cranialward the difference is not marked. This impression is borne out by our results.

RESULTS OF TREATMENT

Of our 88 patients, 15 survived five years or more. This gives an over-all absolute five-year survival rate of 17 per cent. Of these 15 patients, ten were living at the time of this review, one more than five years, two more than six, four more than seven, and three more than ten years after treatment. Thirteen patients could not be traced and are presumed dead of their disease. If these patients are excluded from the final analysis the relative five-year survival rate becomes 20 per cent.

Twenty-five patients (28 per cent) survived for more than three years. The relative three-year survival rate excluding untraced patients is 33 per cent.

For one reason or another ten of the 88 patients received incomplete or markedly curtailed treatment of less than four days' duration. Some had changed their minds after treatment was begun and decided

TABLE VI

FIVE-YEAR SURVIVAL RATE AS RELATED TO DOSE AND TYPE OF LESION

	TOTAL		5-YR. SURVIVAL	
	PATIENTS	PER CENT	PATIENTS	PER CENT
High dose	21	24	4	19
Low dose	67	76	11	16
Type of lesion				
Lymphosarcoma	4	5	1	25
Lympho-epithelioma	59	67	13	22
Squamous cell epithelioma	17	19	0	0
Miscellany	8	9	1	12
Total	88		15	17

to return home for treatment; some had complications which forced discontinuation of therapy. Among these ten were five who received only a single intranasopharyngeal application of radium. If these ten, incompletely or minimally treated, patients are excluded from our series, the absolute five-year survival rate becomes 19 per cent.

In view of our revised thinking concerning the advisability of higher tumor doses (since the completion of this series) and with regard to the generally held view that higher tumor doses will yield a proportionately higher salvage rate, it was of interest to attempt some comparison of tumor doses. As an arbitrary dividing line we chose a mid-plane tumor dose of 3500 r in three to four weeks. Dosages in excess of this amount were referred to as "high doses," of less than this amount as "low doses." In marked contrast to our present management of nasopharyngeal malignant lesions, only 21 (24 per cent) of the 88 cases received high dose therapy, 67 (76 per cent) receiving what today is considered suboptimal dose levels. The salvage rates between the two groups of patients differed little (Table VI).

This experience is in accord with that of Lenz who was of the opinion that tumor dose was definitely not the deciding factor in the outcome of treatment.

Our experience along with that of Lenz fails to indicate that the salvage rate, at least in nasopharyngeal malignant lesions, is

TABLE VII

FIVE-YEAR SURVIVAL RATE AS RELATED TO INITIAL MORPHOLOGY

SITE OF INITIAL LESION	TOTAL CASES	5-YR. SURVIVAL PATIENTS	5-YR. SURVIVAL PER CENT
Confined to nasopharynx	20	6	30
Dissemination to regional nodes only	41	6	15
Base of skull invaded or cranial nerve involved only	11	3	27
Both regional nodes and bony invasion with or without involvement of cranial nerves	14	0	
Systemic dissemination	2	0	

dependent on the tumor dose. Calculation of the dose in our series has been complicated by the topical use of radium in the nasopharynx in the majority of cases reviewed. Obviously with the rapid fall off in relative depth dose from topically placed radium, it is relatively impossible to estimate average volume dosage. For example, the usual topical application of radium consisted of the direct apposition of two 50-mg radium tubes filtered with 1 mm of platinum on a T applicator directly against the primary lesion for six hours. Thus 600-mg hours afforded a surface dose of 13,000 r and a dose at 1 cm of only 2000 r. The exact point at which such surface treatment should be evaluated remains a matter of conjecture and we have chosen to ignore the surface contribution of such treatment in attempting to evaluate the over-all effectiveness of externally administered roentgen therapy. Our choice was based primarily on failure to find evidence that such surface therapy added anything to the over-all salvage rate. Sixty-four patients (73 per cent) were treated with the nasopharyngeal application of radium in conjunction with externally administered roentgen therapy. The five-year survival rate in this group was 17 per cent, not different in any respect from that of patients who received external therapy alone.

Again in agreement with most reported series, the type of lesion has been found to play a most important role in the determination of salvage rates. Without exception the five-year survival rates in the lympho-epithelioma and lymphosarcoma groups have exceeded those in the squamous cell epithelioma group by two or three to one. Among the 17 patients with squamous cell epitheliomas in our series, in 16 of whom the lesions were highly undifferentiated (grade 3 to 4 Broders' classification), not a single one survived five years (Table VI).

As might be expected, the extent of dissemination of the disease when first discovered influences to a considerable extent the ultimate prognosis (Table VII). Of all patients with regional nodal dissemination, 11 per cent survived five years, and of all with bony invasion of the floor of the middle fossa or cranial nerve involvement or both, 12 per cent survived five years.

While our results, 17 per cent over-all five-year survivals, do not compare with the best that have been reported to date, it can be hoped that further refinements of technique, earlier diagnosis and better understanding of the biologic variabilities involved will lead to a significant improvement in survival rates (Table VIII).

TABLE VIII

COMPARATIVE RESULTS OF TREATMENT OF NASOPHARYNGEAL CANCER

	5-YR. SURVIVAL RATES, PER CENT
Lenz	27.6
Nielsen	24
Stout and associates	16.6
Martin and Blady	25
del Regato	18.4
Godtfredsen	22.2
Simmons and Ariel	9.8
Graham and Meyer	19
New and Stevenson	13
Present Mayo Clinic series	17

SUMMARY

Eighty-eight cases of primary nasopharyngeal malignant disease encountered at the Mayor Clinic during the years 1945 through 1949 have been reviewed. The disease is found in the very young and very old, the extremes in our series being five and 78 years with an average age of 45.5 years. Eighty per cent of our patients were male, a sex predominance in accord with most reported series. The lesions in 19 per cent of the cases were squamous cell epitheliomas, in 67 per cent

lympho-epitheliomas, in 5 per cent lymphosarcomas, and in 9 per cent a miscellany including small cell carcinoma, cylindroma and others not classified.

The exact point of origin of 53 per cent of these lesions could not be determined either because of the large bulk of the primary lesion or because adequate clinical description was lacking. Of the remaining lesions, 29 per cent arose from the region of the fossa of Rosenmüller, 46 per cent from the vault, 10 per cent from the anterior wall of the nasopharynx and 15 per cent from the posterior wall. There was apparently no greater tendency to regional dissemination from any particular site of origin than from any other site.

The tumors in 23 per cent of these cases were confined to the nasopharynx proper at time of diagnosis. In 47 per cent they had spread to involve the regional cervical nodes, in 12 per cent there was evidence of cranial nerve involvement or destruction and invasion of the floor of the middle fossa, in 16 per cent both of the foregoing types of dissemination were present and in 2 per cent there was evidence of distant or systemic spread only. The initial symptoms were reviewed in the light of the various modes of tumor dissemination.

The sarcoma group, including the lymphomas, lympho-epithelioma, and transitional cell epithelioma, have a greater tendency to invade the regional nodes than do the squamous cell epitheliomas. Both groups at least in our series tended to invade superiorly producing bony destruction of the floor of the middle fossa or paralysis of cranial nerves with about equal facility although the squamous cell epitheliomas had a slightly greater tendency to metastasize in this manner.

Roentgenologically demonstrable destruction of the floor of the middle fossa in the region of the foramen lacerum was noted in 11 of the cases reviewed. This figure would undoubtedly have been higher but for the fact that stereoscopic views of the base of the skull were not obtained in all cases.

When nasopharyngeal malignant lesions invade superiorly through the foramen lacerum, the VI and V cranial nerves are most frequently involved. When the disease disseminates posteriorly and laterally through the retromandibular and retropharyngeal spaces, the IX, X, and XII cranial nerves are most commonly affected.

Results of treatment indicate an over-all absolute five-year survival rate of 17 per cent. Surprisingly there was no apparent corre-

lation between survival rates and magnitude of the tumor dose administered, an experience also reported by others. All of the five-year survivors belonged to the sarcoma or lympho-epithelioma groups, as none of the 17 patients with squamous cell epithelioma survived five years. The five-year survival rate was 30 per cent when the disease was confined to the nasopharynx, 15 per cent when it had extended to the regional nodes only, 27 per cent when it had advanced superiorly and destroyed the floor of the middle fossa or involved the cranial nerves, and 0 when both types of metastatic spread were present. Survival for five years in all cases of involvement of the regional nodes was 11 per cent, and in all cases of involvement of either bone or cranial nerve was 12 per cent.

Intranasopharyngeal topically applied radium apparently added nothing to the salvageability of this group of nasopharyngeal carcinomas.

MAYO CLINIC

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LXXVI

STUDIES IN SIALOLITHIASIS II: URIC ACID CALCULUS OF THE PAROTID GLAND:

REPORT OF A CASE

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Gout, a disturbance of uric acid intermediary metabolism, is a clinical entity which has been known to the physician since the days of antiquity. It is characterized by: 1) arthritis; 2) hyperuricemia; 3) tophi-deposits of uric acid crystals in articular, periarticular and subcutaneous tissues; 4) late renal and cardiovascular complications.[1]

The uric acid tophus in the ear, the hallmark of gout, has frequently been observed by the otolaryngologist. However, it has been of only passing interest to him since this telltale white nodule in the helix of the ear is hardly the principal problem of the patient suffering from this dyscrasia.

Soft tissues some distance removed from the vulnerable articular structures are not commonly involved except for the kidneys.[2] There are, however, a number of isolated cases in which uric acid deposits have been recovered and identified chemically in atypical areas of the body. These include the tongue, epiglottis, vocal cords and arytenoid cartilages[3]; the eye[4]; valves of the heart[4] and myocardium[5]; and the corpus cavernosum and prepuce of the penis.[6] These uric acid or urate collections are unusual since none of the structures mentioned, except the kidney, are associated physiologically with uric acid excretion.

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However, there is another organ in the body where uric acid is not only deposited, but is actively excreted in sufficient quantity to be of importance both physiologically and clinically. This organ is the parotid salivary gland. The clinical problem is the parotid swelling associated with the formation of uric acid salivary stones which the otolaryngologist may be called upon to diagnose and treat. The physiological problem is the possible role of the salivary gland in the excretion of uric acid and its relationship to the metabolic disturbance which results in gout. An investigation of the latter is beyond the scope of this presentation, but the clinically observed gouty calculus of the parotid gland, heretofore not described, is of noteworthy significance so that definition of its clinical, radiographic and physico-chemical features is in order.

REPORT OF A CASE

L.V., No. 800173, a 54 year old housewife, was admitted to University Hospital on December 13, 1954, for evaluation and treatment of tophaceous gout of 10 years' duration. One year prior to admission the patient noticed sudden onset of pain and swelling in the left parotid region while eating. The swelling subsided gradually, but never completely. Two days prior to admission she had another episode of painful parotid swelling while eating. There was no complaint referable to the opposite side. An otolaryngological consultation was requested.

Examination revealed a well nourished white female with obvious tophaceous gout involving both ankles, the right knee and upper tibia, both elbows, the wrists and the fingers (Fig. 1). Typical deposits in the helix of the ears were not present. The left parotid gland was markedly enlarged (Fig. 2), and tender to palpation. Massage stimulation produced clear saliva from each parotid and submaxillary salivary gland. Further examination was confined to the left parotid gland at the patient's request. Stensen's duct was probed with Bowman's olive-tipped lacrimal probes to 2 cm from the orifice where a solid obstruction was encountered. Bimanual palpation, with the probe in place, gave the impression of a large calculus in Stensen's duct. A No. 4 blunt-tipped lacrimal probe (Williams') was inserted in an attempt to displace the stone. Yellow granular chips were expressed from the duct orifice. This material was placed on a glass slide and mixed with a few drops of the patient's own parotid saliva for microscopic examination. Stensen's duct was then catheterized with a P. E. No. 60 polyethylene catheter preparatory to sialography.

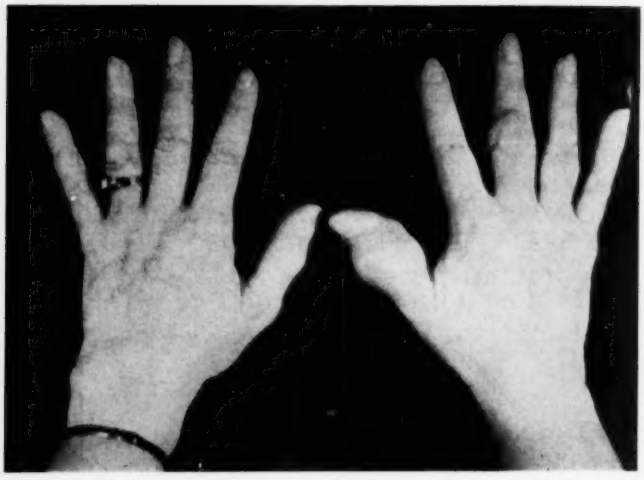

Fig. 1.—Gouty arthritis (case L.V.) characterized by swollen and misshapen joints with tophi.

Fig. 2.—Case L.V., a 54 year old housewife with tophaceous clinical gout and a uric acid calculus of the parotid gland.

TABLE I

PRINCIPAL ORGANIC AND INORGANIC CONSTITUENTS OF PURE PAROTID SALIVA

(PARAFFIN STIMULATION)

STUDIES	CASE L.V. WITH URIC ACID STONE	RANGE OF NORMAL VALUES	CASE WITH CARBONATE-APATITE STONE (PAROTID)
ph	6.0	6.01 - 7.05	8.17
uric acid (mg%)	11.5	1.0 - 5.7	5.5
creatinine (mg%)	0.35	0.11 - 0.54	0.37
total protein (gm%)	0.23	0.12 - 0.42	0.16
bicarbonate (as CO_2 combining power in Meq/L)	1.80	7.0 - 17.0	8.1
sodium (Meq/L)	3.0	4.0 - 14.1	6.0
potassium (Meq/L)	27.9	19.4 - 25.4	24.0
chloride (Meq/L)	22.2	14.0 - 22.4	13
calcium (mg%)	4.7	1.0 - 3.4	2.0
phosphorus (mg%)	17.0	12.2 - 17.4	13.0
volume of secretion (ml. per hour)	6.0	5 - 8	5.5

Pure parotid saliva was collected from the patient in the fasting state. Stimulation of salivary flow was by continuous chewing on paraffin.

Laboratory data: Microscopic examination of the gravel chipped from the calculus revealed the quadrate forms of uric acid crystals (Fig. 3). The murexide test for uric acid was positive.[8] No cells or organisms were found on microscopic examination of the parotid saliva prepared by the methylene blue or Wright's stain. The culture yielded no growth. The various chemical constituents of pure parotid saliva and other material collected from the patient is shown in Table I. The serum uric acid was 11.5 mg per cent (5.5 mg per cent is the upper limiting value for the normal female); urate and creatinine clearance studies indicated impaired renal function.

Sialographic studies utilizing the technique of secretory sialography[9] were performed on December 16, 1954.

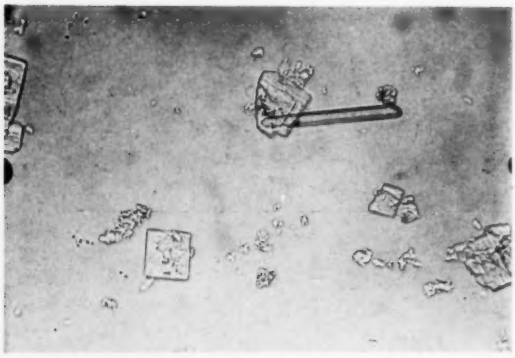

Fig. 3.—A photomicrograph (75x) of the colorless, square or rectangular uric acid crystals taken from the gravel expressed from orifice of left Stensen's duct.

Scout films: The screening films in either P-A or lateral projection showed no evidence of a radiopaque calculus (Fig. 4).

Filling Phase: Following the injection of 1.7 ml of Pantopaque,® a large radiolucent calculus (approximately 1.5 x 1.25 cm) was lodged in a dilated segment of Stensen's duct (Fig. 4).

Emptying phase: The P-A film following attempted emptying by stimulation by lemon showed retention of the contrast material in the dilated main duct surrounding the large calculus. The stone appeared to be larger than demonstrated in the filling phase due to partial emptying of contrast material over its superior portion (Fig. 4).

This sialographic pattern was compatible with a radiolucent parotid duct calculus which chemically appeared to be composed of uric acid.

Course: Upon admission to the hospital the patient was started on anti-gout medication. She was given colchicine, 0.6 mg, twice a day after meals and orally administered cortisone, 5 mg, four times a day for eight days without any noticeable effect on the size of the parotid swelling. The patient was discharged for the Christmas holiday and removal of the stone was planned via the intra-oral route in January, 1955. Medication to be taken at home included probenecid,

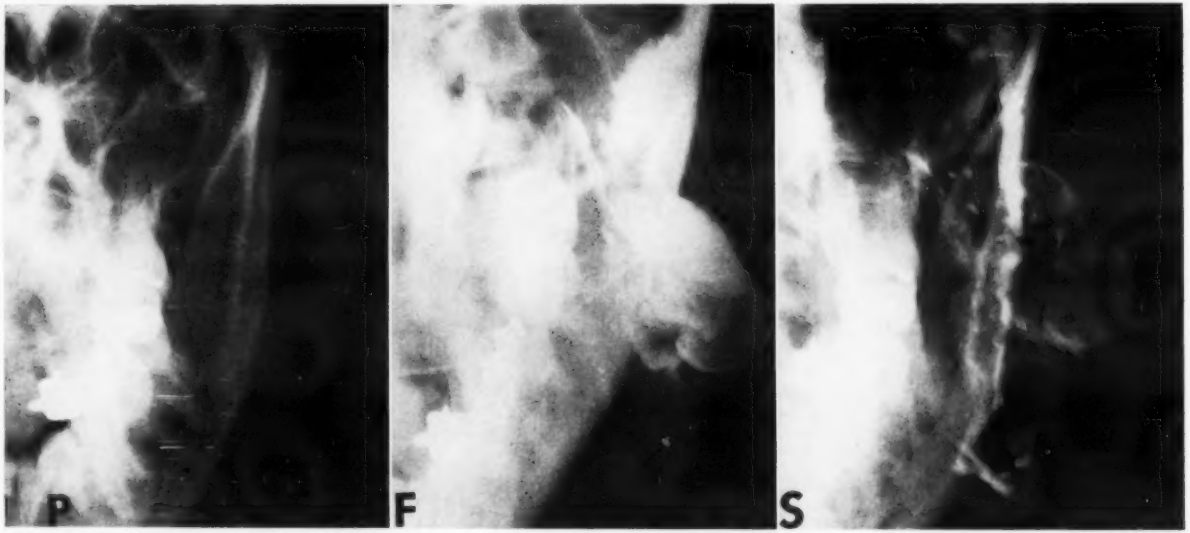

Fig. 4.—Sialogram of case L.V. The scout or preliminary film (P) shows no evidence of a radiopaque calculus. However, the filling phase (F) demonstrates a large radiolucent shadow in a dilated segment of Stensen's duct. Attempted emptying by lemon stimulation (S) shows retention of contrast material in the dilated main duct surrounding the large (approximately 1.5 x 1.25 cm) radiolucent calculus.

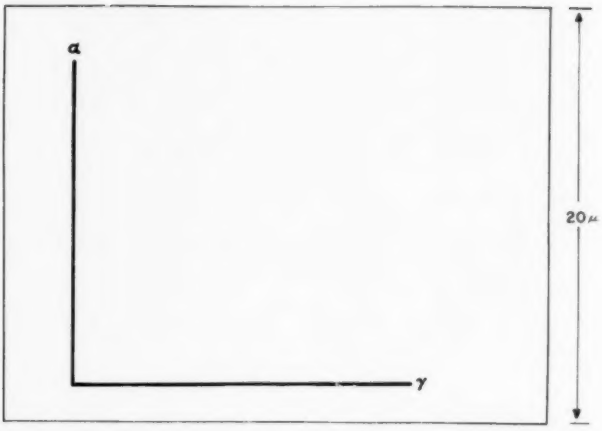

Fig. 5.—Optical properties of stone chips obtained from case L.V.: Colorless, rectangular, orthorhombic plates, parallel to (001) bounded by (010) and (100). Plates have parallel extinction and show a centered flash figure in convergent light. Interference color between crossed polars, third order green. Indices of refraction are $\alpha = 1.57$ and $\gamma = 1.83$. The plates average 20μ on an edge and about 5μ in thickness. These data are characteristic of uric acid crystals. These crystals show a different habit from those illustrated by Prien and Frondel.[11]

0.5 gm, twice a day, cortisone, 5 mg, four times a day, and colchicine, 0.5 mg, three times a day.

The patient was readmitted in January, 1955, and the above three medications were continued in the same dosages. On January 13, 1955, she was seen by the otolaryngological consultant. The patient stated that there had been a somewhat bitter taste in the mouth almost daily for two weeks. Examination revealed no evidence of parotid swelling or calculus by palpation or probing. The saliva from the left parotid gland was crystal-clear. The patient is being treated and followed by the arthritis section at regular intervals. To date there have been only two subsequent episodes of parotid enlargement (bilateral), neither of which have caused pain or interference with eating.

COMMENT

The structural characteristics and composition of salivary gland calculi as described by Blatt, Denning, Zumberge and Maxwell[10] indi-

TABLE II

X-RAY DIFFRACTION SPACING DATA

CHIPS FROM PATIENT		URIC ACID STANDARD	
d (Å)	I	d (Å)	I
6.7	s	6.7	s
5.6	w	5.6	w
4.89	s	4.89	s
3.86	s	3.86	s
3.29	m	3.29	m
3.19	m	3.19	m
3.09	vs	3.09	vs
2.87	m	2.87	m
2.79	vw	2.79	vw
2.57	w	2.57	w
2.24	w	2.24	w
2.18	w	2.18	w
		1.97	vvw
1.87	vvw	1.87	vvw
1.79	w	1.79	w

This table gives the interplanar spacings as measured for the stone chips taken from the patient's left parotid gland and for known standard uric acid. The spacings are given in angstrom units and are represented as d(Å). The relative intensities (I) are expressed as very strong (vs), strong (s), medium (m), weak (w), very weak (vw) and very, very weak (vvw). The patterns were made in a camera of 114.7 mm in diameter with Cu radiation filtered through Ni foil. The x-ray tube was operated at 30KV and 15 MA. Exposure time was 5 hours. Photographs of the actual patterns are also presented in Figure 6.

cate that the usual salivary gland calculus is composed of carbonate-apatite, $CaCO_3(Ca_3)PO_4)_2)x$, a complex carbonated calcium phosphate, which can be identified by chemical, optical and x-ray diffraction methods.

Material, taken from this patient in the form of chips or gravel, is pure uric acid: 2,6,8-trioxypurine, $C_5H_4N_4O_3$. This is verified by the microscopic appearance of the uric acid crystals (Fig. 3), the optical properties of the crystalline chips (Fig. 5) and the x-ray diffraction powder photograph and spacing data (Fig. 6 and Table

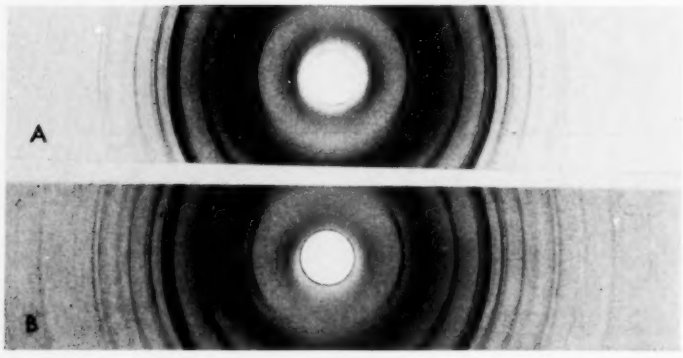

Fig. 6.—(A) X-ray diffraction (powder) photograph of the crystalline uric acid taken from the orifice of Stensen's duct. The pattern is distinctive with many sharp lines. (B) The powder pattern obtained from known standard uric acid. Both photographs are virtually identical.

II). These findings are in agreement with those of Prien and Frondel[11] who indicate that uric acid occurs most often in urinary calculi in the pure state. Obviously, our observation awaits further proof since the analysis has not been made upon an intact calculus. Thus the structural characteristics of a uric acid salivary gland stone are also not definable. There is additional evidence, however, that these chips appear to come from a pure uric acid stone formed in the duct of a salivary gland and that this formation is probably caused by a metabolic error which results in an increase in serum uric acid and a corresponding increase in parotid salivary excretion. Table I shows that the uric acid of the pure parotid saliva from the involved gland is at least twice the concentration of uric acid in pure parotid saliva from a normal individual or from a carbonate-apatite-stone former. The acid pH of saliva and the diminished CO_2 combining power, factors which create an acid medium for the precipitation of uric acid, is further evidence that uric acid deposition is possible in a salivary gland.[12]

The uricosuric action (promoting urinary secretion of uric acid) of probenecid was negligible in this patient because of impaired renal function. Thus, the serum urate level was not reduced and the urate deposits in the articular structures or in the subcutaneous tophi did not diminish in size. Yet, the persistent bitter taste in the mouth while on probenecid therapy, associated with the failure to demonstrate

the calculus found four weeks previously, suggests that the calculus was gradually dissolved.

SUMMARY AND CONCLUSIONS

A patient with tophaceous clinical gout and a uric acid calculus of the parotid gland is presented.

Since the calculus appears to be radiolucent upon routine roentgenographic examination, sialography is a valuable diagnostic aid for its detection.

The crystalline composition, as determined by chemical, optical and x-ray diffraction analysis of chips taken from the stone, appears to be pure uric acid.

Factors which create an acid medium favoring precipitation of uric acid in the salivary gland are an elevated serum and salivary uric acid, a low CO_2 combining power and an acid pH. Uric acid calculus formation in the parotid salivary gland should be included in the list of potential complications of gout.

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LXXVII

INVERSE BONE CONDUCTION

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Los Angeles, Calif.

An objective method of testing hearing mechanisms has long been desired by both otologist and audiologist. An approach to such a test for the middle ear elements is described herewith.

INVERSE BONE CONDUCTION—ANIMAL EXPERIMENTATION

Much of our work at the Deafness Research Laboratory at the Children's Hospital in Los Angeles has been concerned with the measurement of cochlear microphonics in animals. In this connection we have consistently measured both air and bone conduction simultaneously, and these measurements indicate that bone conduction varies considerably with the condition of the middle ear elements.

Figure 1 shows a progressive loss due to perforation of the eardrum, both in bone conduction and air conduction. The upper bone conduction curve shows an extensive anterior perforation; the second bone conduction curve, immediately below it, shows the eardrum completely excised. After the eardrum was excised, the oval window was blocked by dental cement, causing a further loss. The loss of response for bone conduction is obviously very much less than that shown for air conduction, but the loss is still a function of the condition of the middle ear; thus it was reasoned that this change in bone conduction must be due to a very close coupling between the inner and middle ear elements, such that the condition of one is reflected directly into the other. Since the coupling is so tight, it seemed likely that sound pressure levels might be developed in the external auditory canal by movement of the eardrum, due to bone conduction excitation.

Preliminary tests on human subjects made in January of 1956 indicated that this was true; a measurable signal could be developed

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From the Deafness Research Laboratory of the Children's Hospital.

Supported in part by grants from the National Institute of Neurological Diseases and Blindness, U. S. Public Health Service and the Central Bureau of Research of the American Otological Society.

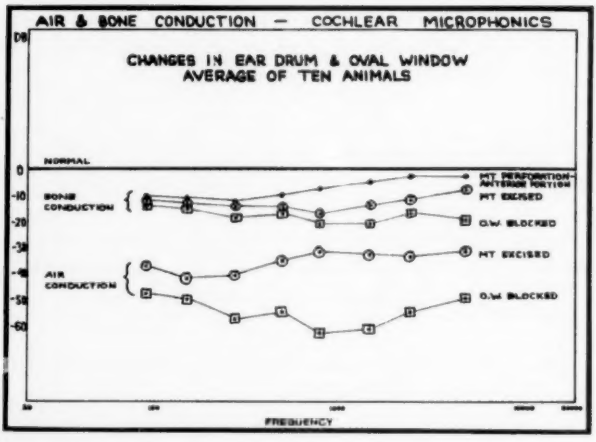

Fig. 1.—Average variations in bone conduction due to middle ear changes in the cat. Air conduction under the same conditions is shown for comparison.

in the external auditory canal from bone conduction excitation of relatively high levels, applied either to the forehead, to the vertex, or to the mastoid. A number of questions immediately presented themselves as to the source of this sound pressure level, a) whether it is due to an inertial effect of the ossicles, b) whether it is due to distortion and consequent change in volume of the tympanic cavity, or c) whether it is due to distortion of the otic capsule reflected through the ossicular chain to the eardrum. Questions of this type are better answered in experimental animal studies than in human studies.

The equipment used in this work has been essentially standardized for the measurement of cochlear microphonics, and has been described by us[1,2] as well as many others. It consists essentially of a signal generator, an amplifier, an attenuator and a vacuum tube voltmeter, which is used to measure constant voltage across the bone and air conduction receivers. For air conduction the receiver is a Telephonics Extended Range No. W3-ARR unit, the bone conduction receiver being a Western Electric D-80904 unit.

A tube from the air conduction receiver is sealed directly into the auditory canal of the animal under test, and the bone conduction

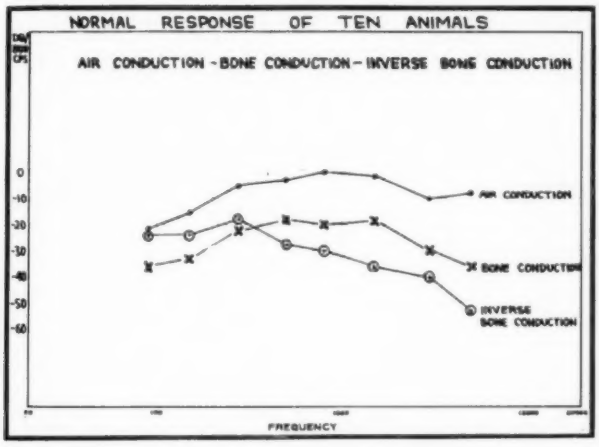

Fig. 2.—Comparison of measured frequency response characteristics in air conduction, bone conduction and inverse bone conduction of the cat.

unit is placed directly on the skull without intervening tissue. An electrode is implanted on the lip of the round window and the cochlear microphonics then are picked up by this electrode, amplified in a 60 db pre-amplifier, and measured in a General Radio Frequency Analyzer No. 736A, which acts as a 5 cycle wide band pass filter over the audible range. The signal can be taken from the 736A analyzer, passed through a log type amplifier, and chart recorded for a continuous record when desired.

Figure 2 compares the average normals of three different types of response, all from the same ten animals. The responses for air conduction and bone conduction were both measured by cochlear microphonics. The response from inverse bone conduction, that is, the sound pressure level appearing in the auditory canal from bone conduction excitation, was measured by a calibrated condenser microphone sealed into the canal by Tygon tube. This tube is 1/16 inch bore and eight inches long. Lamb's wool is lightly distributed inside the tube for damping. The condenser microphone is an Altec 21-D unit which is calibrated for measuring sound pressure levels. The voltage output of the microphone is 50 db below 1 volt per dyne per cm,^{2} and the free field frequency response for the microphone is flat within 1 db between 50 and 4000 cycles. The Tygon tube was used to permit a flexible coupling between the auditory canal and the

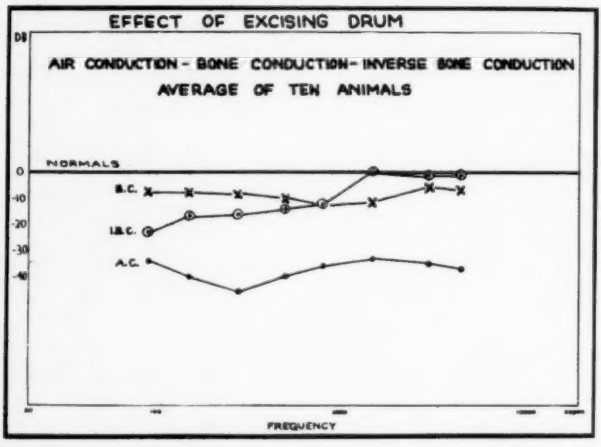

Fig. 3.—Average difference in response from the normals of Figure 2, caused by excising the ear drum.

microphone that would not transmit appreciable vibration directly from the bone conduction excitation. The relatively thick wall of this tube (1/16 inch) reduces the loss at high frequencies while retaining considerable flexibility. However, there is a 6 db per octave loss due to the tube and damping.

In Figure 2 the air conduction transducer functioned at an input voltage 20 db below that of the bone conduction unit. The response of this transducer is thus shown as being 20 db higher at 800 cycles, the mid-frequency. Using the same method of approach, the bone conduction unit was excited 10 db higher for inverse bone conduction than for normal bone conduction. The inverse bone conduction is thus shown 10 db below the normal bone conduction response at 800 cycles. The inverse bone conduction response, uncorrected, drops sharply with frequency, and between 250 and 3000 cycles, shows the expected drop of approximately 6 db per octave over the critical speech range, due to the probe tube and damping. A signal from a standard audiometer cannot be used for this type of test, since the normal threshold equalization is an additional 10 db per octave over approximately this same range.

For these animal tests, the bone conduction unit was always applied directly to the bone at the junction of the occipital and

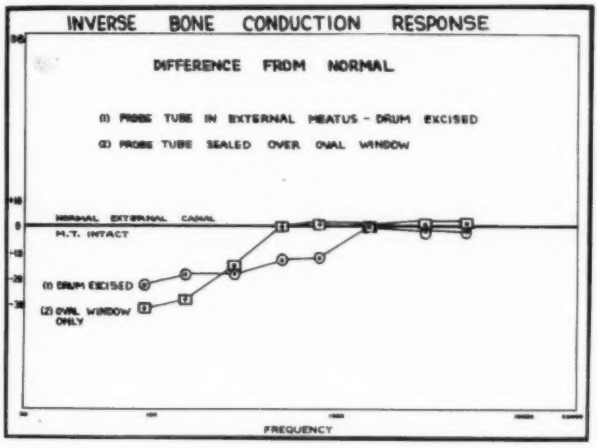
INVERSE BONE CONDUCTION RESPONSE
DIFFERENCE FROM NORMAL
(1) PROBE TUBE IN EXTERNAL MEATUS - DRUM EXCISED
(2) PROBE TUBE SEALED OVER OVAL WINDOW
NORMAL EXTERNAL CANAL
M.T. INTACT
(1) DRUM EXCISED
(2) OVAL WINDOW ONLY
FREQUENCY

Fig. 4.—Comparing the average response measured by inverse bone conduction under two conditions: (A) Response in the external meatus when the eardrum is excised. (B) Response from the oval window only—probe tube sealed over stapes.

lambdoidal ridges. The vibration transmitted from the bone conduction unit is made to be essentially parallel to the plane of the eardrum. Since the skull of the cat is quite thin over most of its area, it is considerably more subject to resonance than the skull of the human; consequently, most of the head tissues were left intact on the skull to serve as damping. Tests with the bulla open or closed indicated little difference in response for this test.

One of the most radical things that can happen to the middle ear and its structures is the loss of the eardrum. In this case, removing the eardrum also indicates how much of the sound pressure level generated in the external meatus due to inverse bone conduction is caused by this membrane. Figure 3 shows the effect of excising the eardrum, both on air conduction (A.C.), bone conduction (B.C.) and inverse bone conduction (I.B.C.). Each of these values are plotted as differences with respect to their own individual normals. Thus a single line labeled "Normal" is actually representing the three different normals previously shown in Figure 2.

In inverse bone conduction, or for convenience I.B.C., the maximum loss due to the removal of the eardrum is at the low frequencies,

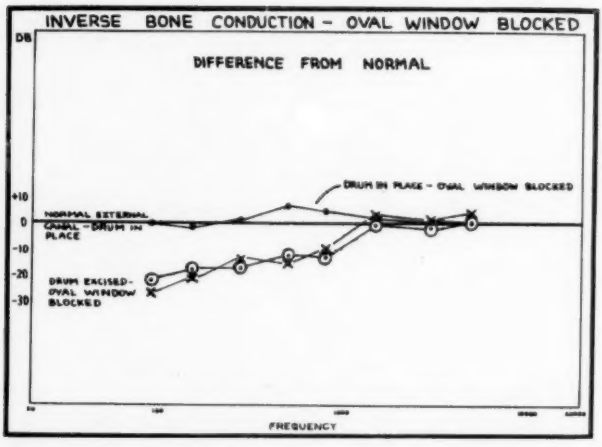

Fig. 5.—Blocking the oval window makes little difference in response when the ear drum is missing, but raises the midfrequency response when the drum and ossicles are intact.

which is to be expected. Very little loss is shown above 1500 cycles. The inverse bone conduction response shows considerably less spread in individual measured results than the cochlear microphonics, particularly of bone conduction. Also, the wave shape is somewhat cleaner. However, inverse bone conduction is, of course, subject to all of the ills which beset normal bone conduction; that is, change of contact pressure, differences in the amount of tissue which lies between the bone conduction receiver and the skull, and the shape and area of the applicator of the bone conduction unit.

Figure 4 shows the same graph as in Figure 3 of the response due to inverse bone conduction when the eardrum is excised. In addition to this graph, and for direct comparison to it, a second curve is shown in which the I.B.C. response is measured when the probe tube is sealed directly over the oval window, the ossicles thus being completely eliminated as well as the space of the tympanic cavity. This was done to discover, if possible, how much energy was being radiated by the footplate of the stapes. From the data in Figure 4 it would appear that a considerable amount of energy is being radiated between 1500 cycles and down to 300 cycles. This response is partially dissipated in the tympanic cavity and external meatus when these areas are open to the oval window.

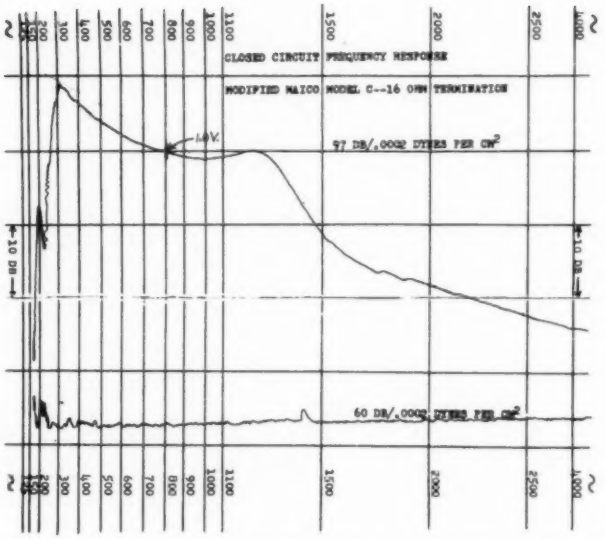

Fig. 6.—Frequency response and signal to noise ratio of the system used in human tests of inverse bone conduction.

It also appears to be true that the tympanic cavity or the ossicular inertia, or both, are contributing something at the very low frequency end to the energy measured in the external canal, since when this cavity is eliminated, there is some drop in response below 250 cycles.

Several attempts were made to determine, if possible, how much of the energy measured in the external canal was contributed normally by ossicular inertia, but results as measured on the cat were erratic and inconclusive. The anatomy of the cat, and particularly that of the middle ear structure, is so different from the human that information obtained in this manner would have had questionable value in application to the human.

Figure 5 shows that when the eardrum is excised, an oval window block has relatively little effect; the difference noted being plus and minus and apparently random. A peculiar condition arises, however, when the oval window is blocked with normal drum and ossicles in place. Here the response, as shown, actually increases in the mid-frequency range. This increase seemed initially to be highly improbable, and additional experimental animals were used to verify

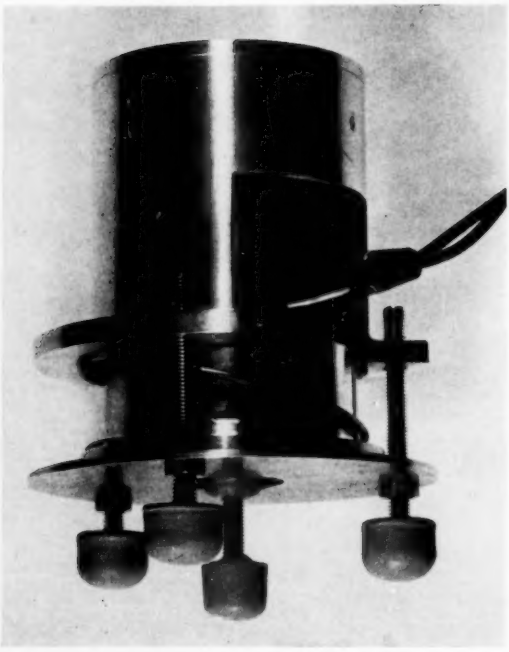

Fig. 7.—Bone conduction transducer—Modified Maico "C" unit. The three outer feet are fixed to the case. The center foot is the applicator which is pressed back against a spring until the outer feet all contact the head.

it; thus the averages here are for more than ten animals. Since this mid-frequency rise covers a fairly wide frequency range, it is probably not due to some phase aiding effect. However, the condition observed could be due to removal of the hydraulic damping of the inner ear fluids, or it may be that this is the reverse of the effect, long noted, that the bone conduction threshold is apparently lowered when the external auditory canal is occluded. This could be explained in the following manner: normally the inertial action of the ossicles is free to radiate energy both to the cochlea through the stapes, and to the external auditory canal through the eardrum. In our experiment we immobilized the stapes, and thus all the inertial energy appeared at the eardrum. Even a partial block of the auditory canal would have the reverse effect of radiating more of the inertial

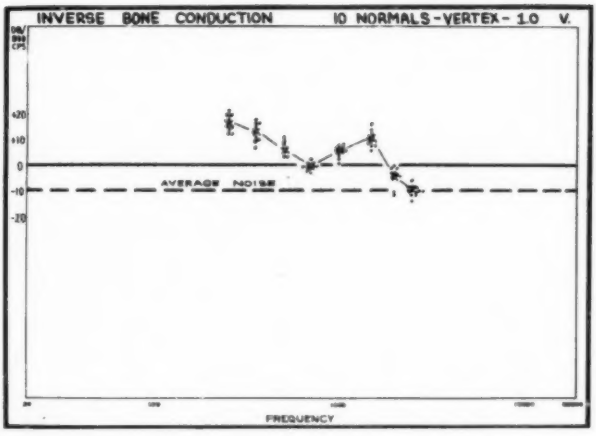

Fig. 8.—Inverse bone conduction measured on ten adults with essentially normal hearing. The spread is about that of bone conduction threshold measurements.

energy toward the cochlea. This theory can be checked by comparing normal cochlear microphonics with the response when the external meatus is occluded.

From the data acquired from animal experimentation, it would appear that the sound pressure level appearing in the external auditory canal from bone conduction vibration is probably caused by a combination of three factors: 1) ossicle inertia; 2) distortion of the tympanic cavity; 3) distortion of the otic capsule which radiates very little energy except through the ossicles to the intact eardrum. These three different signal "sources" may phase in and out with respect to each other, and produce a ragged type of response with changing frequency. A further and more detailed study of these possible phasing effects may yield valuable information; however, with our present knowledge they appear to be more confusing than instructive.

To summarize the animal experiments on inverse bone conduction, the following appears to be true:

1. Frequency response as measured is mostly at the low frequency end; very little response over 2500 cycles.

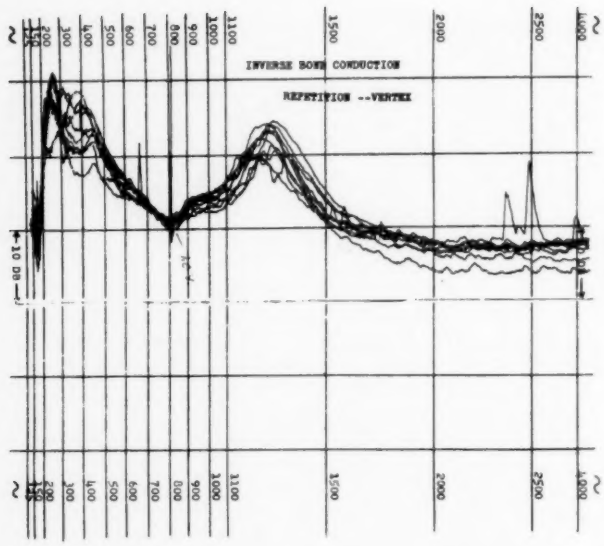

Fig. 9.—Repetition characteristic of inverse bone conduction on the same ear. The variation is 5 db above 500 cps and about 10 db below this frequency.

2. Loss of the eardrum drops the low frequency response of inverse bone conduction.

3. Added oval window block after the loss of the eardrum does not materially change the response.

4. Sealing a probe tube on the oval window indicates that the footplate of the stapes radiates some mid-frequency energy.

5. Blocking the oval window, with the ossicles and drum intact, raises the mid-frequency response above normal.

INVERSE BONE CONDUCTION—HUMAN SUBJECTS

Since starting this project, a preliminary report[3] by Andersen, Holmgren and Holst of Stockholm has described this test method and gives some data obtained from human subjects, but without attempt at evaluation of the test method as an audiologic tool.

The area and the force of application of the bone conduction unit is as important in inverse bone conduction as in threshold bone conduction tests. The highest signal level is obtained from application of the signal on the mastoid, but this area for inverse bone conduction is inclined to be erratic, and critical to direction of application, indicating the ossicular inertia effect. Probably, also, there is some direct contamination of the sound pressure levels due to actual distortion of the external canal and from applicator contact with the cartilage of the ear, etc.

The vertex of the skull is a preferred area, and while it is about 10 db lower in output level for the same excitation, this point of application is preferred over some other places such as the forehead, since the most probable field of application for inverse bone conduction is in patients that are under general anesthesia. The vertex also has the advantage that it is relatively accessible in surgery without violating sterile techniques.

Figure 6. The power required for good response in inverse bone conduction is about 20 db above the maximum normal audiometer output for bone conduction. This value is not maximum, but rather a minimum amount for reasonable signal to noise ratio.

The hearing aid type of receivers are in general not suited to this order of power, and the Western Electric D-80904 receiver used on animals is too cumbersome for convenient use in human tests. The Maico Model C "laboratory type" receiver has been used for this purpose in a modified form, and the frequency response of the overall system using this unit is shown in Figure 6.

The response characteristic of Figure 6 was obtained by closing the ear end of the microphone tube and applying the bone conduction applicator to the wall of this plastic tube under constant pressure. After the upper curve of Figure 6 was traced, the transducer was lifted just clear of the microphone tube. The transducer was again excited at the same level through the same frequency range to determine the noise and acoustic crosstalk level which is shown in the tracing at the bottom of Figure 6. The excitation was 10 db below that used in clinical bone conduction. It will be noted that the response peaks at 300 cps and again at 12 to 13 hundred cps and drops at about 9 db per octave. This fairly smooth response was obtained by driving the unit from a 16 ohm source terminated in a 16 ohm resistor. Figure 7 shows the modification of the unit for constant force and direction of application on the vertex or forehead.

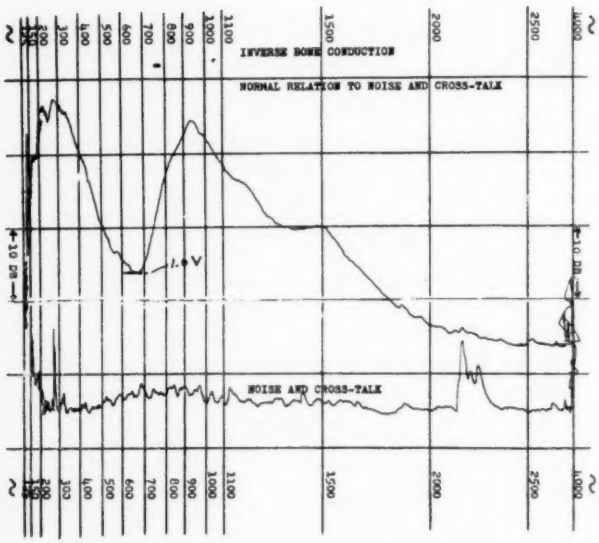

Fig. 10.—The relation of signal to noise-frequency calibration is incorrect.

Figure 8 shows the average frequency characteristics obtained from ten normal human ears, and the spread of individual response. The variations are about the same as reported by Andersen et al[3] and about what would be expected from conventional bone conduction audiometry.

Figure 9 is an actual chart of individual response, testing the repeatability of the vertex location using the modified Maico Model C receiver with 1.0 volt across the transducer at 800 cps. Normal operation is carried out at a level 10 db higher (3.16V) than that used in these tests. The transducer begins to overload at about 4 volts. The ear tested in Figure 9 shows a typical response obtained from normal ears.

The signal level to the transducer is necessarily so high that it radiates considerable ambient noise. Figure 10, showing noise and cross talk, indicates that relatively little of the ambient signal is picked up by the probe tube and microphone. Figure 10 is similar to the graph of Figure 6, except that the I.B.C. response shown in the upper curve is that of a normal ear and the frequency calibration

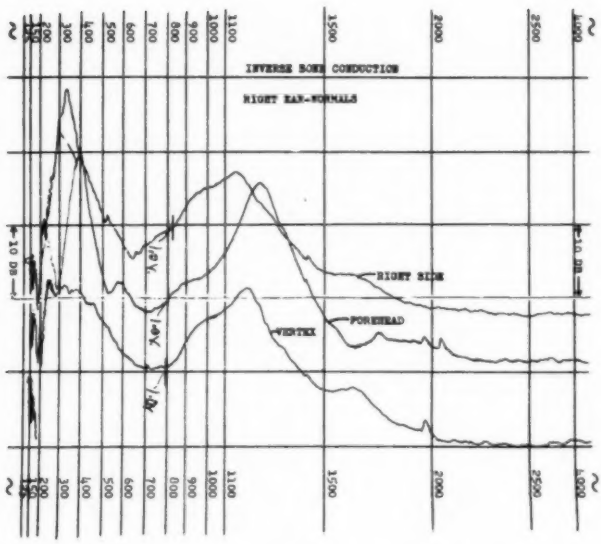

Fig. 11.—Relative response of the same ear to three different positions and directions of application of the bone conduction transducer.

is incorrect. The lower tracing was made with the transducer lifted just clear of the head but maintained in place. The sudden change in noise level shown between 2000 and 2500 cps was caused by a slammed door.

Figure 11 shows the response of a normal ear to bone conduction applied to the head in three different places and involving application of the vibratory force in three different axes with respect to the head. The transducer excitation was the same at 800 cps in each case, but the reference position of each tracing is separated by 10 db for identification. The forehead response is typically high in resonance peaks. In general, the response from the vertex and side of head above the ear is not materially different except at the low frequencies.

The real test of inverse bone conduction as a clinical tool is whether conductive losses can be measured in the human with any degree of accuracy. In stapes surgery we have conductive losses which can be tested at different stages by both conventional audiometry and inverse bone conduction: tests can be made with the eardrum normal and again after the eardrum has been opened. The effect of a

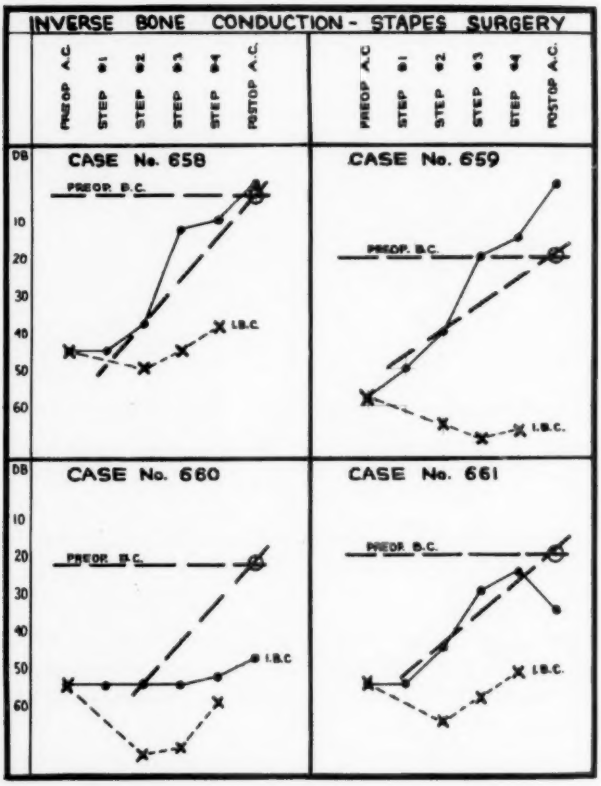

Fig. 12.—Comparison of response from air conduction audiometry and inverse bone conduction under conditions of stapes surgery.

blocked stapes can be measured, and later the effect of a mobilized stapes. Such tests have been made on a very limited scale, but unfortunately they are somewhat contradictory.

Figure 12 shows the responses of four consecutive stapes mobilization surgery cases with the audiometry test results displayed in nomograph[4] form.

For "I.B.C." test during surgery, the bone conduction receiver is held in position on the patient's vertex by a nurse. This can be

done beneath the sterile sheet without violating sterile techniques. The flexible plastic tube which seals into the patient's ear and connects to the microphone can be sterilized, and thus several such tubes can be used in successive tests.

Inverse bone conduction was measured in each case before surgery and this measurement is then comparable as a base line with the usual preoperative air and bone conduction tests. A second test on inverse bone conduction is made at Step 2, where the eardrum is open. A third test is made at Step 3, after the stapes has been mobilized or mobilization attempted, and a fourth test is made at Step 4, after the drum is back in place. These inverse bone conduction tests are made immediately after the usual surgical audiometry, and thus we have direct comparative tests between air conduction and inverse bone conduction.

For convenience in comparing the inverse bone conduction with air conduction, it is desirable to provide inverse bone conduction with some single figure of merit, such as that used in the nomograph display showing the progress of surgery. For convenience, the sound pressure levels measured by the condenser microphone in the external meatus were related in decibels to one millivolt and the mean of all the readings at each half octave step from 125 to 2000 cycles per second was used as a single figure to represent the relative change in response from test to test. In this manner comparison can be made with simultaneous data derived from air conduction excitation.

Preoperative air conduction and preoperative inverse bone conduction provide a common starting point, thus if we align the two results at this point, we can tell whether inverse bone conduction is varying in such a direction and by an amount which would indicate the different known conditions of the middle ear.

CASE NO. 658. This is a fairly typical case of successful mobilization. Inverse bone conduction shows an expected drop at Step 2, where the middle ear is opened (ear drum reflected) while the response increases at Step 3. (This does not agree with the test data from animals (Fig. 5) where blocking the stapes made little difference when the eardrum was not functioning.) At Step 4 a further increase in response is measured, and again this condition does not appear to follow the results of Figure 5 where the over-all response was greater when the stapes was fixed with the drum normal. Thus Step 4, where the stapes has been freed, should show a lower sound pressure level than the preoperative condition. This, of course, may

be modified by the fact that the eardrum after surgery is essentially loose and therefore more responsive to the low frequency excitation of I.B.C. than in the normal preoperative state.

CASE NO. 659. This is also a successful case, although the nomograph displays an unusual shape. Inverse bone conduction, however, does not follow the progress of mobilization as in Case No. 658, and is somewhat closer to the characteristics shown by animal tests.

CASE NO. 661. This patient was also successfully mobilized in surgery, but showed some regression at the first postoperative test. Inverse bone conduction in this case seems to follow the same characteristic as in Case No. 658.

A composite characteristic of ten successful cases shows a consistent drop at Step 2, where the eardrum is open, a rise at Step 3 and little change at Step 4 which averages about the same level as the preoperative test. The standard deviation is between 6 and 6.4 db at the three measured steps.

CASE NO. 660. This case apparently failed to mobilize in surgery although the first postoperative test shows 15 db gain indicating that some degree of mobilization must have occurred. The I.B.C. Response seems to follow the known condition fairly well.

CONCLUSIONS

The above four cases and the seven others which are at hand are obviously too few to justify firm conclusions. However, from the data that we now have on inverse bone conduction as applied to the human ear, inverse bone conduction does not appear to reflect accurately the conductive condition of the middle ear. It seems likely that the uncertainty involved stems from the fact, as previously noted in connection with animal experiments, that the response is a resultant of at least three different interacting paths of acoustic energy. Thus the response may depend on which path predominates. While this is confusing at the moment, and appears to render the tests unreliable, it may be possible as further data is collected to sort out the various factors and their predominance so as to provide information of value.

SUMMARY

Sound pressure levels produced in the external auditory canal by bone conduction vibration of the skull are evaluated by means of

animal experiments and also by tests on the human patient in the various stages of stapes mobilization surgery. From limited information available at this time, this method of measuring the mechanical condition of the human middle ear mechanism does not appear reliable.

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LXXVIII

UREA EXCRETION THROUGH THE HUMAN SALIVARY GLANDS

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The purpose of this work is to compare the blood urea level with that of the saliva in order to clarify the ways in which the urea passes from the blood to the saliva, there being most probably only a passage and not an autocthonous formation of urea. In the event that the concentration of urea is greater in the saliva than in the blood, the finding would be susceptible to interpretation only by admitting either a reabsorption of the liquid part in some tracts of the adenomere, or an active secretion of urea in some tracts of the adenomere itself.

In any case, the explanation would imply a functional pattern of the salivary glands, consisting either in the reabsorption of the liquid component of the saliva, or in an active secretion of urea perhaps only in certain portions of the adenomere itself.

The comparative study of the concentration of urea in the blood and in the saliva has been the object of numerous investigations and it cannot be said that the results have led to any definite conclusions, although the notions acquired have been of a certain interest.

Urea has been found in the saliva as far back as 1873 by Rabutteau.

In the determination of salivary urea care must be taken to always take into consideration the ureasic activity of the numerous germs which make up the bacterial flora of the oral cavity. Above all, those results must be taken into consideration in which the determination has been done either on the saliva immediately after

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it has been gathered, or on the saliva which has been preserved at very low temperatures or by means of substances meant to impede its enzymatic hydrolysis.

These precautions and those regarding the methods of measurement lead to a critical evaluation and a selection of the results to be found in the literature. To the results, for example, obtained by measuring the urea gasometrically by oxidation with hypobromites there cannot be given any appreciable scientific value. At the most, they can be of only approximate value.

Desgrez, Moog and Gabriel,[6] using hypobromite, have obtained values which are higher than those obtained by using xanthydrol. And thus also for Vladesco[30,31] and Maupetit.[13,14] For this reason, one remains perplexed as to what value to attribute to the results and affirmations of Vladesco and Popesco,[32] of Vladesco[30,31] and Scarpulla.[22]

With the urease method, Schmitz[24] found in saliva an average urea content of 5-12 mg %, and this is, according to this author, in such constant relationship with the blood urea concentration that the latter can be calculated through the determination of the saliva urea level in 88% of the cases. The affirmations of this author are not adequately supported by his own experimental results. He calculated the urea concentration from the colorimetric determination of the NH_3, liberated from urea in the presence of urease, with Nessler's reagent (Schmitz).[24,25]

Successively, Landsberg,[12] Updegraf and Lewis,[29] Desgrez, Moog and Gabriel,[6] Schultz and Ziegler,[23] Peracchia and Trinchera,[19] Miyasaki Shoichi,[15] Trettenero,[28] Weinberger and Peola,[33] Binet and Marek,[4] Fernandez and Guardiola[8] arrived at fundamentally concordant results in normal subjects and in subjects with higher azotemic values.

Morris and Jersey[16] saw that the urea content (= NH_3 plus amino-acids) varies directly with the volume of saliva secreted. Since NH_3 varies irregularly with the rate of saliva secretion, the authors inferred that the presence of NH_3 in the saliva depends on factors other than the activity of the gland. Since after chewing paraffin the volume of the saliva increased by 429% while the concentration of NH_3 varied by 729%, that of urea plus 734%, that of creatinine by 118% and that of uric acid by 63%, it was logical to think that the ways in which these substances passed into the saliva should have depended on different factors. If the flow of saliva was made to

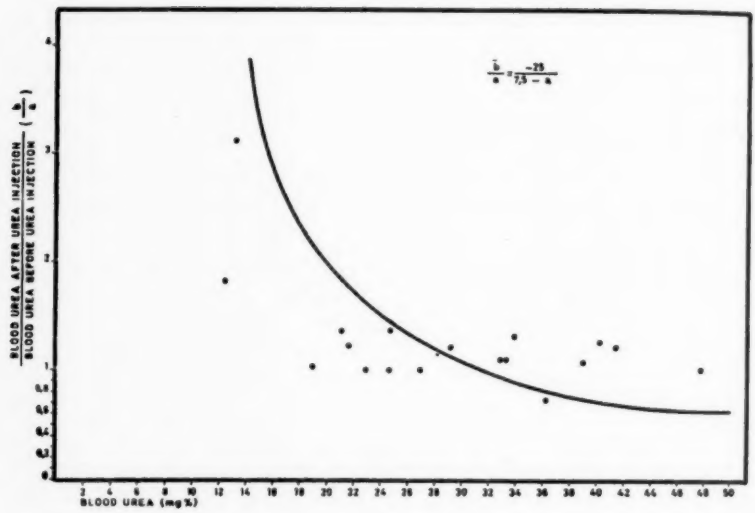

Figure 1

increase reflexly by dripping a dilute solution of acetic acid into the mouth, the volume increased by 56% while the concentration of NH_3, of urea, of creatinine and of uric acid increased respectively by 302%, 200%, 124% and 71%.

The increase in concentration is therefore very variable for all of the substances tested except for uric acid. The volume of the saliva increases more than the concentration of the substances dissolved in it. After injection of pilocarpine, the volume of saliva secreted per hour increases by 502%, and the concentration of uric acid by 183%; the increase in concentration lasts longer for uric acid than for the other substances which return rapidly to normal. Atropine acts in a manner exactly opposite to pilocarpine. These results lead to the belief that not all of the substances reach the saliva by means of simple filtration from the blood.

The content of uric acid in the saliva is, according to Morris and Jersey, an expression of the nucleoproteic metabolism of the saliva secreting cells and not the result of a mere filtration.

The influence of pilocarpine, arecholine and atropine on the quantity and chemical composition of saliva has been studied by several other authors.

Vladesco and Popesco[32] saw the hypobromite nitrogen of saliva to pass from 260-476 mg to 131-327 mg after injection of pilocarpine in man, while the corresponding blood variations passed from 217-372 to 279-372 mg; the hypobromite nitrogen tends therefore to fall in the saliva and to maintain, on the contrary, an almost constant level in the blood.

The affirmation of these authors, according to which xanthydrolic nitrogen does not exist in normal saliva and appears instead in abundance after administration of pilocarpine, seems curious enough: the pilocarpine would successively sensibly reduce the NH_3 level of saliva. Since NH_3 is utilized in the process of ureogenesis, in order to explain the obtained experimental results, the authors advance the hypothesis of an eventual utilization of NH_3 for urea formation in the salivary glands.

More interesting seem the results of Barnett and Bramkamp,[1] who put the rate of secretion of saliva in relationship to its content in urea and NH_3. The spontaneous slowly secreted saliva of 16 normal subjects contained 44 mg % urea when the salivary secretion rate was 0.47 ml/min. If, by chewing paraffin, the salivary secretion rate was accelerated from 0.47 to 3.97 ml/min, the urea content of saliva was lowered to 22.7 mg %. The parotid saliva, secreted under reflex stimulation with tartaric acid at a secretion rate of 13.9 ml/min, contained 22.1 mg % of urea, while the slowly secreted saliva (0.31 ml/min) contained 29.3 mg % urea.

By contemporaneous determination of the blood urea level it was possible to observe that in slow secretion the salivary urea level is 1.22 times more concentrated than in the blood, while in rapid secretion it is only 0.76 times the blood urea.

These values refer to the total saliva. For the parotid saliva the corresponding values are 0.85 times in slow secretion and 0.73 in rapid secretion.

The increase in the salivary urea level over the blood urea level cannot be explained except by admitting either a reabsorption of the liquid part of the saliva in some portions of adenomeres, or an

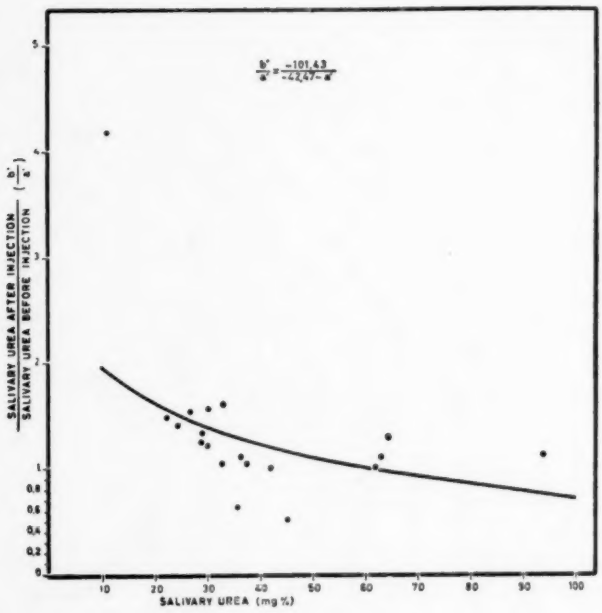

Figure 2

active secretion of urea, or finally a synthesis of urea in the adenomeres themselves.

Since it could not be explained why urea should be more actively secreted during slow secretion of saliva it was more logical to admit a reabsorption of the liquid part whenever the saliva remains in the excretary ducts for a longer period of time. Bergmann,[3] in contrast to Peracchia and Trinchera,[19] has been able to ascertain that the diminution of the percentage content of urea in the saliva after injection of pilocarpine is proportionate to the increase in the quantity of saliva secreted, so that the quantity of urea secreted remains practically constant in successive units of time.

Pilocarpine should therefore only displace but not modify the equilibrium of concentration between the blood urea and that of the saliva; the urea blood level is lowered by pilocarpine injection although to a lesser degree than the salivary one. Atropine generally

brings about modifications in the urea content of the saliva opposite to those caused by pilocarpine, although not with absolute constancy. Binet and Marek[4] saw the blood and salivary urea level increase contemporaneously after the second injection of pilocarpine. The increase occurred earlier and was higher in the saliva than in the blood.

By studying contemporaneously the total quantity of saliva secreted and its percentage content of urea and chlorides, Bramkamp arrived at the conclusion that the total quantity of urea excreted through the salivary glands is not influenced either by pilocarpine or by atropine, while the concentration of chlorides is influenced by both of these alkaloids. The processes relative to the secretion of chlorides and urea are therefore different, there being probably a process of filtration for urea and of true secretion for the chlorides.

According to Rossi and Daubard,[21] the blood urea level remains constant after injection of pilocarpine while the level of urea in the saliva is modified in relation to the phase of secretion.

A good part of the above cited researches clearly allows one to glimpse the possibility that the level of urea in the saliva is modified in relation to the various phases of salivary secretion itself. Besides some of the authors cited above, Simmel and Kuntscher,[26] Binet and Marek,[4] Vladesco and Maupetit[13,14,30,31] agree, although without committing themselves decisively on the intimate causes of this phenomenon.

Naturally, if a substance is found in the saliva in higher concentration than in the blood, before proceeding to a deduction on the intimate mechanism of the finding it is imperative to orientate oneself on the origin of the substance itself, on whether it reaches the saliva from the blood or on whether it is formed, wholly or partly, in the cells of the gland itself.

The deductions are obviously different according to the case.

Reference has already been made to the experiments of Morris et al. relative to the presence of uric acid in saliva. Updegraf and Lewis[29] found it in saliva in concentration equal to 40% that of the blood, and Maupetit[14] also held the uric acid concentration in the saliva to be such a faithful expression of the blood uric acid concentration that the one could be calculated from the other.

Haida Shigeo[10] saw saliva uric acid concentration remain practically constant in rabbits injected with pilocarpine, and to increase if

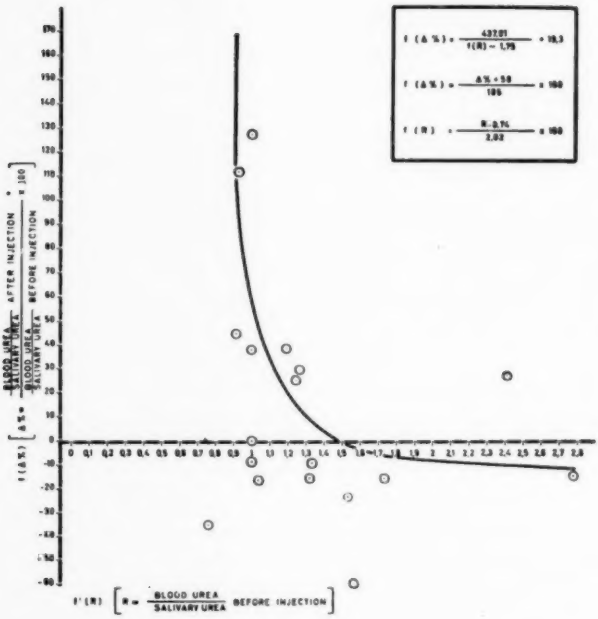

Figure 3

the pilocarpine was preceded by an injection of atophan. Bauriedel[2] did not believe that a relationship could be established between uric acid concentration in the blood and in the saliva. Although they arrived at results which were different from those of Morris and his colleagues,[16,17] Murakya, Yamaguchi and Kobayashi arrived at the same conclusion, that is, that uric acid like NH_3 reaches the saliva through a process which is not a simple filtration.

From the preceding there emerges: a) that urea is secreted into the saliva through a process of simple filtration, and therefore the knowledge of the relationships between its concentration in the blood and in the saliva in the most disparate experimental conditions represents a valid index for the knowledge of the intimate mechanisms responsible for the passage of urea into the saliva; b) that uric acid, like NH_3, creatinine, the phosphates ecc., represent in the saliva, wholly or partially, the products of the metabolism of the gland cells themselves.

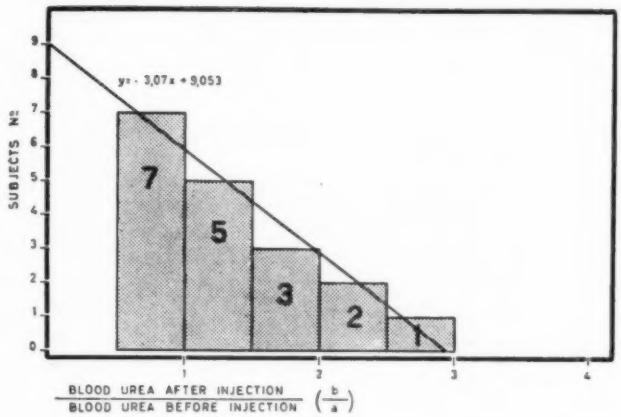

Figure 4

For this reason there cannot exist any fixed and constant relationships between the levels of these latter substances in the blood and saliva, since they depend contemporaneously on processes of filtration and on metabolic factors, at least one of these latter entities being unknown and difficult to determine (cellular metabolism) both qualitatively and quantitatively.

In the attempt to arrive at the complex from the simple in the study of one aspect of the physiology of the salivary glands we have executed the simultaneous determination of the urea levels in the blood and saliva of human subjects. It seemed convenient to us to gather the saliva not in conditions of exaggerated activity, which would have represented an element of difficult evaluation in the glandular secretion itself. We have instead preferred to vary the hematic urea level by injecting, intramuscularly or intravenously, congruous quantities of urea and determine simultaneously and at fixed time intervals after the injections, the urea level in both the blood and the saliva.

Experiments of this sort had been made as far back as 1928 by Gosman, who injected urea into normal subjects and into subjects with kidney diseases while soliciting the secretion of saliva by chewing boli of paraffin.

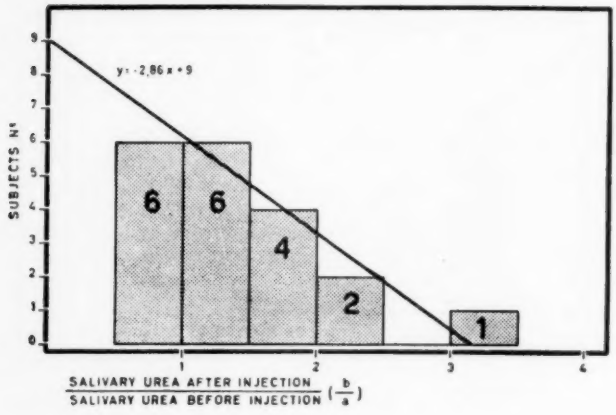

Figure 5

In these experiments, after injection of 20 gr of urea, the concentration in the tissues increased by more than 50% within a period of time in which from 25% to 33% of the administered urea had already been secreted. Twelve hours after the administration, the blood urea level was still slightly above normal, while 24 hours later it went down to the point of departure. This did not occur in the subjects with kidney diseases. According to Gosmann,[9] urea presents constant levels in the saliva as long as the water metabolism remains equal and perfectly equilibrated.

Higher values of blood urea were encountered in patients with kidney disease by Schultz and Ziegler,[23] and in children convalescing from pneumonia and empyema by Falkenheim.[7]

Simonini[27] saw the saliva urea level rise in children on a hyperproteic diet, and diminish in those on a hypoproteic diet.

TECHNIQUE OF OUR EXPERIMENTS

The experiments were performed on a total of 19 subjects, of which 8 were men, in good general condition except for two who had active renal disturbances.

From the fasting subject peripheral venous blood was taken and at the same time the total saliva was gathered after detersion of the

tubes after being filtered through sterile gauze. Both the blood and saliva were analyzed either immediately after they were gathered, or in the morning, after 24 hours, the latter samples being preserved oral cavity with running water. The saliva was gathered in dry test under refrigeration for 24 hours.

Coagulation of the blood was impeded with potassium oxalate.

Immediately after taking the first sample of the venous blood an injection was made intramuscularly with 5 ml of a 1.8461% iso- and in the saliva, was done by means of the urease method and tritionic solution of urea in bidistilled water in the first two experimental subjects, of 10 ml of the same solution intramuscularly in the third subject, and of 15 ml of the same solution intramuscularly in the fourth subject.

In four subjects, 10 ml of a 25% urea solution was injected intramuscularly and in eleven subjects this quantity was given intra- and in the saliva, was done by means of the urease method and tritivenously. The determination of the urea level, both in the blood metrically, titrating the exact quantity of NH_3 given off in bubbles in the presence of cold concentrated K_2CO_3 in a known volume of a titrated solution of acid containing a few drops of an indicator (methyl red). Practically, the method of Van Slyke and Cullen was followed. The urease was suspended day by day, in a 1/15 M phosphate buffer solution and was always added in quantities which were several times higher than those needed in order to hydrolyze, in the determination, all of the urea contained in the volume of blood or saliva which was brought into contact with it.

The incubation lasted 20 minutes and the strong current of environmental air, deprived of eventual traces of volatile alkali by being bubbled through a concentrated solution of H_2SO_4, was successively passed for 30 minutes through 30 ml of a 0.02 NH_2SO_4 solution, always exceeding the equivalents of NH_3 which was developed.

The quantities of blood or saliva analyzed were either 1 or 2 ml, according to the relative availability. Almost all the analyses were conducted twice and the obtained values were always concordant.

RESULTS

1) *Modifications of the Blood Urea Level After Intramuscular or Intravenous Injection of Urea.* The herein reported results appar-

ently deviate from the argument which was proposed. However, since the modification of the urea level of the saliva was followed parallelly before and after intramuscular or intravenous administration of urea, the consideration of the modifications of the blood urea was rendered necessary.

The results are given in Table I.

TABLE I

MODIFICATIONS OF THE BLOOD UREA LEVEL BEFORE AND AFTER TREATMENT WITH UREA

NO.	METHOD OF TREATMENT WITH UREA	BLOOD UREA (MG.%) BEFORE (A)	AFTER (B)	B / A
1	5 ml. 1.8461% sol. I.M.	24.48	24.48	1
2	5 ml. 1.8461% sol. I.M.	24.48	33.66	1.37
3	10 ml. 1.8461% sol. I.M.	38.9	42.—	1.08
4	15 ml. 1.8461% sol. I.M.	33.86	45.251	1.33
5	10 ml. 25% sol. I.M.	39.92	51.—	1.27
6	10 ml. 25% sol. I.M.	41.289	50.265	1.22
7	10 ml. 25% sol. I.M.	18.85	19.55	1.04
8	10 ml. 25% sol. I.M.	47.75	48.47	1.01
9	10 ml. 25% sol. I.V.	29.17	32.39	1.11
10	10 ml. 25% sol. I.V.	29.17	35.60	1.22
11	10 ml. 25% sol. I.V.	22.74	22.74	1
12	10 ml. 25% sol. I.V.	12.32	22.74	1.84
13	10 ml. 25% sol. I.V.	36.13	26.73	0.74
14	10 ml. 25% sol. I.V.	21.59	26.73	1.24
15	10 ml. 25% sol. I.V.	20.94	27.23	1.34
16	10 ml. 25% sol. I.V.	33.18	36.13	1.08
17	10 ml. 25% sol. I.V.	26.73	26.73	1
18	10 ml. 25% sol. I.V.	32.99	36.13	1.09
19	10 ml. 25% sol. I.V.	13.16	41.88	3.18

If the values of the relationships (A, Table I) obtained as functions of the initial blood urea level are examined, it can be seen (Fig. 1) how with the decrease of the initial blood urea level there is a progressive increase in the relationships themselves. The fall of these relationships is at first rapid, then slower. The relationship tends asyntotically to infinity for values of the blood urea level at the limit of 7.5 mg%; it tends to 1 for values of the initial blood urea equal to 32.5 mg%. Since the second determinations of the blood urea level were done 30 minutes after the injection of urea, the aforesaid concepts may be interpreted in the sense that the urea rises more rapidly and remains more constantly at the higher level it reaches, for the interval of 30 minutes, the lower was the initial blood urea level, and that when the latter descends below 7.5 mg%, the relationship assumes its maximum values.

If the initial blood urea level were 7.5 mg%, the relationship would tend, theoretically, to become negative; that is, the injected urea would not only immediately disappear from the circulating blood, but it would also tend to eventually take with it the urea which was already present.

Since the relationship becomes 1 for a blood urea level of 37.5 mg% and is very difficult to displace from this value, it signifies that when the blood urea level surpasses the aforesaid limit it can be displaced only with extreme difficulty and remains tenaciously constant because of the efficient and immediate action, evidently, of mechanisms which remove the circulating urea.

2) *Modifications of the Saliva Urea Level After Administration of Urea.* As has already been said above, contemporaneously with the determination of the blood urea, the urea of the total saliva, which was gathered at intervals of time as closely as possible equal to each other, was also determined.

In the following Table II are reported the relative results represented in Figure 2. The curve of the figure demonstrates that the

TABLE II

SALIVARY UREA BEFORE AND AFTER INJECTION OF UREA

NO.	METHOD OF TREATMENT WITH UREA	SALIVARY UREA (MG.%) BEFORE (A)	AFTER (B)	B / A
1	5 ml. 1.8461% sol. I.M.	24.48	33.8	1.38
2	5 ml. 1.8461% sol. I.M.	37.30	39	1.04
3	10 ml. 1.8461% sol. I.M.	51.76	51.76	1
4	15 ml. 1.8461% sol. I.M.	93.5	106.36	1.13
5	10 ml. 25% sol. I.M.	52.8	57	1.07
6	10 ml. 25% sol. I.M.	42.24	42.18	0.99
7	10 ml. 25% sol. I.M.	22.14	32.42	1.46
8	10 ml. 25% sol. I.M.	36.60	22.73	0.63
9	10 ml. 25% sol. I.V.	45.25	22.73	0.5
10	10 ml. 25% sol. I.V.	29.17	35.60	1.22
11	10 ml. 25% sol. I.V.	29.02	37.69	1.49
12	10 ml. 25% sol. I.V.	12.32	51.79	4.2
13	10 ml. 25% sol. I.V.	32.99	51.79	1.57
14	10 ml. 25% sol. I.V.	26.73	40.93	1.53
15	10 ml. 25% sol. I.V.	36.29	39.41	1.08
16	10 ml. 25% sol. I.V.	30.05	47.09	1.56
17	10 ml. 25% sol. I.V.	64.32	81.86	1.27
18	10 ml. 25% sol. I.V.	32.99	34.56	1.05
19	10 ml. 25% sol. I.V.	29.92	35.90	1.2

level of urea in the saliva is modified according to a pattern fundamentally identical to that observed for the blood.

From the algebraic expression of the curve it may be seen that the level of urea in the saliva can increase at the most by 2.39 times ($= \frac{101.43}{42.47}$) at which point it tends to annul itself before the injection of urea.

On the other hand, it does not change when before the injection it tends to the value of 58.96 ($= 101.43 - 42.47$). And finally, it becomes 1 when the level is 58.96. The slowest decrease of the ratio $\frac{A}{B}$ in function of the level of departure of the salivary urea, and the practical absence of an asyntotic for values of the initial saliva urea level tending to zero, demonstrate the strict dependence of the salivary urea level on the blood urea level on the one hand, and the more restricted field of variability of the salivary urea level itself on the other.

In other words, the concentration of urea in the saliva possesses regulatory mechanisms and therefore tends to assume relatively constant values.

Evidently, the excretory function of the salivary glands in regard to urea is neither one of the first nor of the more important functions of the salivary glands themselves, and in this function other excretory organs, like the kidney, play a predominant role.

3) *Relationship Between the Blood Urea Level and the Salivary Urea Level Before and After Dosage with Urea.* The results reported in the accompanying Table III essentially demonstrate a certain tend- urea, is displaced by insignificant values.

If, however, the percentage variations of the aforesaid relationship ($\Delta\% \frac{\text{hematic urea}}{\text{salivary urea}}$) are placed in function of the relationship before dosage with urea, a tendency toward positive values may be observed (Fig. 3), that is, toward an increase in the relationship, and prevalently for low values of the initial relationship itself. There is instead a tendency toward negative values, that is, toward a lowering of the relationship when the initial values are elevated. There exists a discrete variability of the ratios themselves which demonstrate that numerous and variable factors intervene in the regulation of the ratio itself.

TABLE III

RELATIONSHIP BETWEEN BLOOD AND SALIVARY UREA BEFORE AND AFTER DOSAGE WITH UREA

NO.	MG% BLOOD UREA / MG% SALIVA UREA BEFORE	AFTER	Δ% BLOOD UREA / SALIVARY UREA
1	1	1.38	+ 38
2	1.52	1.16	− 23
3	1.32	1.23	− 6.7
4	2.76	2.35	− 15
5	1.32	1.11	− 16
6	1.023	0.84	− 17
7	1.18	1.65	+ 39
8	0.74	0.47	− 36
9	1.55	0.70	− 58
10	1	1	0
11	1.27	1.66	+ 30
12	1	2.27	+127
13	0.91	1.93	+112
14	1.23	1.53	+ 24
15	1.73	1.44	− 16
16	0.90	1.30	+ 44
17	2.41	3.06	+ 27
18	1	0.92	− 8
19	2.27	0.85	− 62

In the passage of urea from the blood to the saliva one must take into consideration not only the permeability of the salivary parenency to the maintenance within certain constant values of the relationship between the blood urea level and that of the salivary urea.

The arithmetical average, in fact, before and after dosage with chyma toward urea itself, but also its variations in the various subjects for the most disparate reasons.

If the subjects whose ratio oscillates within arbitrarily fixed limits are gathered into groups (Figs. 4 and 5), an almost regular diminution in the number of subjects is observed as the ratio between the urea levels before and after dosage increases.

Not so regular, and with a less rapid decrease is (Fig. 5) the progress of the frequencies in the subjects, in function of the ratio between the saliva urea level before and after dosage. These results are purportedly the expression of the great powers of regulation of the urea level in the different individuals.

The ratios between the two urea levels before and after dosage was never greater than 3 in any of our subjects.

The saliva urea level increases after dosage with urea in the greater number of cases. The lowest values are comprised between 0.5 and 1 while the highest values are only slightly greater than 3.

SUMMARY

By means of the reported experiments we have tried to clarify one aspect of the functional activity of the salivary glands through the study of the secretion of urea. The results show that the elimination of urea through the saliva is subject to precise laws and that the elimination itself depends on the conditions of the moment and on individual factors as well as on the blood urea level.

UNIV. DI BOLOGNA

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LXXIX

CARCINOMA OF THE LARYNX

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At a recent symposium on carcinoma of the larynx, sponsored by the American Cancer Society, it was evident that considerable disagreement in regard to the relative indications for surgery and radiation therapy exists. In view of the relatively small number of reports of laryngeal carcinoma treated by radiation therapy in this country, additional reports of the larger series of radiologically treated patients should be made available.[1-5,7-10] With this in mind, a portion of the material on carcinoma of the larynx treated radiologically at the University of California Hospital has been reviewed. At this hospital there has long existed a close co-operation between the members of the Departments of Otolaryngology and Radiation Therapy which has resulted in a policy by which all carcinomas of the larynx are seen jointly by the staffs of the two departments. During the period covered by the present report, most of the therapy was under the supervision of Lewis F. Morrison and B.V.A. Low-Beer. In general, radiation therapy was given preference in all cases in which there was a reasonable possibility of radiologic control. While surgery was used for some lesions in which the vocal cords were fixed and no lymph nodes were present, it was usually reserved for instances frankly thought uncontrollable by radiation, and for the radiologic failures.

The present review analyzes the results in all 124 cases of histologically verified squamous cell carcinoma arising in the endolaryngeal mucosa and treated by primary x-ray therapy during the period from July 1942 through June 1952. This period represents the most recent ten years for which a five-year follow-up is available. Further, the treatment techniques, which were evolving during the preceding years, were relatively uniform at this time. It is for these reasons

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that the 1942 to 1952 interval was chosen even though some of these patients were previously reported.[9] To facilitate comparison between radiologic and surgical series, all cases were reclassified and staged according to the system suggested by Leborgne, as reported by Lederman.[6]

The 124 cases consisted of 96 primary carcinomas of the vocal cord, 26 supraglottic and two infraglottic carcinomas. Supraglottic lesions are those arising from the laryngeal surface of the epiglottis, the false cords, or the laryngeal ventricle. The glottic tumors are those arising from the vocal cords or the commissures. Subglottic lesions arise immediately below the vocal cords and above the level of the cricoid cartilage. The lesions were staged as follows:

Stage I. The carcinoma is limited to the tissue of origin which is freely mobile.

Stage II. The carcinoma infiltrates and may extend beyond the tissue of origin but does not extend beyond the larynx. Mobility of the larynx may be impaired or lost.

Stage III. There is extralaryngeal extension of the carcinoma. This stage includes mobile ipsilateral lymph node metastases.

Stage IV. This stage includes those with contralateral, fixed, or distant lymph node metastases and those with other primary malignant neoplasms previously diagnosed and uncontrolled.

This classification was adopted since it permits direct comparison of radiologic and surgical results. Cases included in stage I can be handled by laryngofissure and cordectomy. Cases of stage II are beyond surgical therapy by cordectomy but can still be treated by total laryngectomy. Stages III and IV are inoperable by total laryngectomy although patients in stage III might occasionally be considered for more extensive surgery.

Most patients were treated through right and left lateral opposing portals. The dose in these cases was calculated in the midplane. A few patients were treated through a single anterior field with calculation of dose at 3 to 5 centimeters below the anterior surface of the neck. In three patients the anterior field was added to the lateral fields because of the skin reaction. The field size varied from 5 x 5 centimeters for lesions limited to the vocal cords to somewhat larger sizes depending upon the size and location of the lesion. Fifty-

eight patients were treated with 1,000 Kvp radiation (9 mm Cu, HVL) to a tissue dose of 5,500 to 7,000 r in 25 to 35 days. In 44 patients treated with 200 Kvp radiation (1 mm Cu, HVL) the tissue dose was 5,000 to 6,000 r in 30 to 40 days. Occasional failure of equipment caused some change from 1,000 to 200 Kvp. Eighteen patients treated since 1949 with 400 Kvp (4.6 mm, Cu, HVL) received tissue doses of 5,500 to 6,500 r in 35 to 40 days. Usually there was an attempt to deliver a midline dose of at least 5,000 to 6,000 r. The preconceived treatment plan was modified in the individual case depending on mucosal and skin reactions and on tumor response as observed by regular examination during the course of therapy.

The results of radiation therapy of the vocal cords are presented in Table I. Of 96 patients, 58 (60 per cent), treated only by x-ray,

TABLE I

RADIATION THERAPY FOR CARCINOMA OF VOCAL CORD

STAGE	NUMBER TREATED	WELL 5 YEARS		LOST CONTACT
		NUMBER	PER CENT	
I	30	24	80	0
II	43	29	67	2
III	19	5	26	0
IV	4	0	—	0
TOTAL	96	58*	60	2

*Two additional patients (one stage II and one stage III) were symptom free seven and 13 years following laryngectomy for recurrence.

were alive and without evidence of disease for five years or more. Although four (two stage I, two stage II) of the 58 with controlled disease had laryngectomy because of the radiation sequelae, nearly all of the other 54 had preservation of good laryngeal function. One patient in stage II and another in stage III survived seven and thirteen years respectively, following laryngectomy for irradiation failure. The over-all salvage rate was 60 of 96 patients, or 63 per cent. Of the 30 patients who could have been treated by a simple cordectomy (stage I), 24 (80 per cent) were controlled by irradiation alone. Of the 43 patients for whom simple cordectomy would not have been

sufficient but who would have been operable by laryngectomy (stage II), 29, or 67 per cent, were five years symptom free. Of the 19 patients in stage III in whom a total laryngectomy would not have been sufficient since the disease extended beyond the larynx, five, or 26 per cent, were salvaged.

In Table II, the five-year survival is tabulated according to the quality of radiation used. From these data there does not appear to be a significant difference in survival when treatment with 200 Kvp, 400 Kvp, and 1,000 Kvp radiation is compared. If there is a difference, it cannot be detected in this series.

TABLE II

CARCINOMA VOCAL CORD

FIVE-YEAR RESULTS FOLLOWING TREATMENT WITH 200, 400, OR 1000 K.V.P.

STAGE	5-YEAR SYMPTOM-FREE / NUMBER TREATED		
	200 KVP	400 KVP	1000 KVP
I	9/13	3/3	12/14
II	8/11	6/8	15/24
III	1/6	1/3	3/10
TOTAL	18/30 (60%)	10/14 (71%)	30/48 (63%)

Of the six patients in stage I who died in less than five years, two remained under regular observation and died without evidence of recurrent laryngeal disease at four years and three months, and four years and seven months, of myocarditis with heart failure and of widespread lymphosarcoma, respectively. Autopsy in the patient who died of lymphosarcoma showed no evidence of recurrence of the carcinoma of the larynx. Two died elsewhere without autopsy and the status of the laryngeal carcinoma is not known. The remaining two had frank recurrence; one was operable but refused laryngectomy, while the other developed inoperable recurrence with extension posteriorly and inferiorly.

Failures in stage II were due to uncontrolled disease. These patients were treated during the first half of the study and it is probable that in some of these laryngectomy would have been performed for the recurrence had they been observed at the present time.

Thirteen patients with advanced or uncontrolled carcinoma required tracheotomy; none of these was classified stage I and none was controlled. In six, tracheotomy was necessary before onset of therapy, and in three others during the first few days of treatment. All four who required tracheotomy after completion of the radiation therapy died of recurrent disease within seven months. Tracheotomy was necessary in one controlled patient six months after therapy for postirradiation edema. In this patient, the tracheotomy tube was removed after ten months and the fistula eventually closed. He is now living 14 years without recurrence of either neoplasm or the laryngeal edema.

TABLE III

RESULTS OF RADIATION THERAPY IN PATIENTS WITH SUPRAGLOTTIC CARCINOMA

STAGE	NUMBER TREATED	WELL 5 YEARS
I	1	1
II	2	1
III	15	2
IV	8	0
TOTAL	26	4

As indicated in Table III, only four of 26 supraglottic carcinomas were controlled. From a review of the records it would appear that probably none of the patients in this group was a good candidate for surgery. These lesions tended to be advanced as indicated by the fact that 23 of the 26 were classified stage III or IV. Interestingly, two of the three stage I and II lesions were controlled. There were only two subglottic carcinomas treated and neither was controlled.

Edema associated with the laryngeal reaction usually subsided within a few weeks when the disease was controlled. Occasionally it persisted for some months after therapy. This has recently led us to protract treatment over a longer period of time or to somewhat reduce the total dose. As mentioned previously, laryngectomy for radiation sequelae with controlled vocal cord lesions was necessary in four cases. Two of the laryngectomies (cord lesions stage I and II respectively) were done because of late chondral necrosis; one (stage I) was for edema which occurred after an upper respiratory infection:

and one (stage II) was for an erroneously presumed recurrence. One patient, 15 months after treatment, developed neurologic symptoms suggesting radiation myelitis. These symptoms have persisted ten years. Three patients developed squamous cell carcinomas within the treated area seven and one-half, eight and one-half, and 12 years after therapy; in the posterior hypopharyngeal wall, on the previously uninvolved vocal cord, and in the piriform sinus, respectively.

SUMMARY

One hundred twenty-four patients with carcinoma of the endolarynx were treated at the University of California Hospital between 1942 and 1952 by primary radiation therapy. Ninety-six were primary lesions of the vocal cord, 26 occurred in the supraglottic, and two in the subglottic areas.

Of the 96 lesions of the vocal cord, 58, or 60 per cent, were controlled by radiation therapy alone. Two radiation failures were controlled by secondary laryngectomy. Of the 31 lesions which could have been treated by cordectomy, 24, or 80 per cent, were living and symptom free at five years. Sixty-seven per cent of the 43 cord lesions that would have required total laryngectomy were controlled by irradiation alone. Five, or 26 per cent, of 19 patients with cord carcinoma, too advanced for control by laryngectomy, were salvaged by radiation therapy.

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LXXX

STRESS FACTORS IN RHINOLOGY

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During the last 25 years the practice of rhinology has changed a great deal due to a better knowledge of functional pathology or pathological physiology, recognition of the part that allergy plays in the nose, introduction of sulfonamide preparations and antibiotics, the newer concepts of emotions, functional disturbances, hypometabolism, better knowledge of the autonomic nervous system and endocrines, especially the steroids and their effect on the nose.

During these times of stress we read and hear a great deal of defenses and chain reactions. These play a great part in the reactions that take place in the nose.

The nose acts as an airway to the lungs and due to its vascularity it has the function of humidifying, warming and filtering out harmful products. The cilia and mucous blanket act as a conveyor system to rid the nose of foreign material. Lysozme has a bacteriostatic effect. Smell is a very important function.

The lining of the nose is derived from ectoderm having the function of being the outer line of defense; so it is richly supplied with nervous elements which adjust rapidly to its external environment.

The rest of the tissues of the nose are derived from mesoderm, for support and transportation being very vascular. The inferior turbinate, especially, having much erectile tissue and being very vascular, swells very easily. It is also rich in collagen.

In the writings of Selye[1] is described the general adaptation syndrome and the local adaptation syndromes as the result of stress which covers many forms of external environment, inflammatory, bacterial or allergic, effects of cold, trauma, weather changes, i.e., humidity,

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changes in barometric pressures, emotional changes, etc. He divides these changes into three phases:

1) The alarm reaction, first, being the state of shock which may include degeneration, necrosis or atrophy, then counter shock which may include acute inflammation, hypertrophy and hyperplasia.

2) The local or general state of resistance which includes chronic inflammation, hypertrophy and hyperplasia.

3) State of exhaustion with degeneration, necrosis or atrophy. As a result of the alarm reaction there is a stimulation of the hypothalmus which controls the emergency and adaptation responses of the body producing a chain reaction which affects the autonomic nervous system and endocrine system by nervous or humoral mediation which produces increased membrane permeability, hemoconcentration, catabolism, hypotension, hypothermia, hyperkalemia; then in the counter phase by hormonal or nervous defense by stimulation of the anterior hypophysis which elaborates ACTH.

The adrenal cortex produces corticoids which stimulate the thymicolymphatic system to produce antibodies, the posterior pituitary to produce vasopressin, the adrenals to produce medulloids and other factors to produce resistance, so when we use vaccines, foreign proteins and injections in allergy, we probably stimulate ACTH production. In inflammatory conditions or acute infections, we will have the following local changes:

1. Disturbance in local fluid exchange.
    a) Increased capillary permeability due to liberation of leukotoxine.
    b) Increase in lymph flow.
2. Localization of irritant (fixation) due to lymphatic blockade by occluding thrombi and fibrinous network. The reaction will also depend on the type of infection and invasiveness.
3. Migration of leukocytes.
    a) Diapedesis of polymorphs due to liberation of leukotoxine.
    b) Increase in ph at site of injury.
    c) Leukocytosis in the general circulation.

Acute infections or toxins generally have the effect of stimulation of the sympathetic system. The hypothalmus registers instantly with pyrexia. Vasomotor centers are affected causing vasoconstriction early; the medulla may respond with nausea and vomiting, the cortex with general malaise, fatigue and mental cloudiness. Hypothalmic centers control blood formation and release leukocytes from the myeloid tissues. The globulin fraction of the plasma proteins is related to antibodies and complements function of the blood plasma. Leukopenia and granulocytopenia are indicative of absence of defense and depression of the bone marrow.

If the toxemia becomes very severe, then we will have vasodilatation, sweating, subnormal temperature, and collapse may appear; so the hypothalmus, autonomic nervous system, endocrines regulate the defense mechanisms. While acute infections have a tendency to produce a general sympathetic stimulation, the substances derived from sensitizing or anaphylactic producing molecules, on the other hand, produce symptoms which indicate a predominance of stimulation of the parasympathetic system, producing a localized effect.

As many changes taking place in the nose in stress are due to nervous vascular changes, I will review the nerve supply of the nose.

Innervation of the nasal membranes and accessory sinuses are supplied by both sympathetic and parasympathetic fibers and sensory fibers from the V cranial nerve. The sympathetic fibers come from the superior cervical ganglion to the sphenopalatine ganglion, then to the tissues of the internal nose.

They cause vasoconstriction to the vessels which supply these tissues, especially in the shock phase or early stage of a cold, causing a dry nose. Later they may dilate or have increased permeability causing increased fluid in the nose. The parasympathetics supply the nasal palatine and pharyngeal mucous membranes and accessory sinuses. These come from the sphenopalatine ganglion from the nucleus of the VII nerve. They course with the fibers of the V cranial nerve. They activate the secreting glands and also have a dilating effect on the blood vessels. So many of the affections of the internal nose have a large autonomic nervous system factor.

Excessive secretion of the glands of the nose and increased permeability of the blood vessels occur in hay fever, acute and chronic rhinitis or sinusitis. While vasomotor rhinitis may be allergic, it often has a large emotional factor. Excess secretions of the nose may be

caused by irritation or reflexes from the eyes, teeth, gastrointestinal disturbances, etc. In these cases the afferent impulse travels in the V nerve or the vagus, then to the VII nerve.

Sneezing is produced by sensory impulses over the V nerve, producing a powerful expiratory effort. It is a defense mechanism.

Pressure in the nose at times will produce reflex asthma through the V nerve to the vagus.

Some of the operations on the nose for asthma have their effect by the stimulation of the sympathetic nerves or production of ACTH, relief of pressures, reflexes and elimination of infections producing an intrinsic allergy. Reflexes through the V nerve to the vagus may also cause slowing of the heart, or to the gastrointestinal tract, producing hyperacidity or spastic constipation or disturbances of menstruation or bladder through sacral parasympathetic reflexes. Herpes of the lips are probably due to a parasympathetic reflex.

Secretory disturbances follow sympathetic paralysis or operations on the cervical ganglia or cord; so increased secretion predominates.

So, in a general way, the sympathetic system prepares the body for flight or fight. It is catabolic in action, while the parasympathetic system is anabolic in its action. Also the sympathetic nervous system stimulates the hypothalmus, pituitary and adrenal axis and the thyroid, while the pancreas and gonads have a stimulating effect on the parasympathetic nervous system; so we can see why drugs or endocrines that stimulate the sympathetic system are used so much in rhinology. Also there is the large neurovascular factor of capillary permeability. This is increased by lack of bioflavonoids, cortisone, prednisolone, vitamins C and P, and calcium.

The endothelium of the blood vessels and mesenchyme, especially of the inferior turbinate, is rich in collagen which has hyaluronic acid as the cement substance. This is acted upon by hyaluronidase producing the spreading factor. The streptococcus is rich in hyaluronidase—so spreads readily, while staphylococcus tends to localize, diphtheria and pneumococcus causing a fibrinous exudate.

During stress there are characteristic changes in the distribution of electrolytes between the cells and the extracellular fluids, changes in the osmotic pressure, acid base balance, renal function and water balance.

Chloride is the chief anion of the extracellular fluid, sodium being the chief cation in extracellular fluids.

Potassium is the chief cation in the intracellular fluid, but only a little is present in the intercellular space, plasma and lymph, but is present in the cell membrane.

Since sodium, the chief basic ion in the extracellular fluid, cannot readily enter the cell, both the osmotic pressure and the ph of the extracellular fluid depend almost entirely on the cation. Acidosis tends to cause dehydration due to diuresis and transfer of water from the plasma to the cells causing swelling of the latter, while alkalosis exerts the opposite effects. So often there is a retention of water in the tissues of the nose, especially in allergies and vasomotor rhinitis. They are helped by increasing the acidity of the nose and body by salt restriction, low sugar, high protein, fat diet, ammonium chloride, low fluid intake, diamox, thyroid, sympathetic stimulants by mouth or nose drops, also by use of hydrocortisone or prednisolone by mouth or nose drops, but if cortisone or prednisolone are used over a period of time, ACTH should be given at least twice a week to prevent adrenal cortical atrophy, i.e., 100 units of ACTH for every 100 mg of prednisone or prednisolone, 100 units of ACTH for every 200 to 300 mg of hydrocortisone or 400 mg of cortisone.

SUMMARY

Stress in its various forms causes profound local changes, but also many systemic ones, due to its effect on the autonomic nervous system endocrines, neurovascular changes, capillary permeability, biochemical changes, electrolyte, acid base equilibrium, water balance, etc. So we must approach rhinology from a much broader viewpoint.

Surgically we should relieve any obstruction, such as a deviated septum or polyps, promote drainage and proper aeration, always trying to conserve the ostium.

Antibiotics, antihistamines, desensitization in allergies, correct autonomic nervous system imbalances, steroids, ACTH, thyroid, as well as proper nutrition, vitamin therapy, especially C, at times low salt diet, and diuretics should be employed. When necessary treat the emotional factor to produce a condition of homeostasis of the nose.

554 Fisher Bldg.

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Scientific Papers of the American Broncho-Esophagological Association

LXXXI

H-TYPE TRACHEOESOPHAGEAL FISTULA

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Congenital tracheoesophageal fistulas of the H-type, that is, without atresia of the esophagus are quite rare but are being reported with increased frequency in the recent literature. Inasmuch as many of the reported cases were diagnosed at autopsy it would seem that this condition has often been unrecognized clinically. Failure to make a diagnosis is usually due to difficulty in demonstrating the fistulous tract between the trachea and esophagus. If the condition is not diagnosed, these infants usually die with recurrent aspiration pneumonia. The diagnosis should be suspected in any newborn with cyanosis and recurrent aspiration associated with feeding.

The first such patient reported in the American literature seems to be that of Lamb[1] in 1873. This fistula was found at autopsy but typical clinical symptoms and physical findings were described. Reference to a similar report appeared later in the same year in the French literature. In 1917 Cautley[2] could refer to only six similar anomalies. By 1954 Ware and Cross[3] could find just 26 cases in the English literature. Six additional reports have appeared since. These, with the two additional cases herein reported make a grand total of 34. Where a large series have been reported there have been two to three patients with the H-type fistula to 100 patients with tracheoesophageal fistulas associated with atresia of the esophagus.

The first surgical repair of this condition was in 1939 by an otolaryngologist, Imperatori.[4] Through a large tracheotomy opening an elliptical collar incision was made around the fistulous opening

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of the posterior wall of the trachea at level of the fifth tracheal ring and then the opening into the esophagus was closed and inverted. The tracheal opening was then closed in a third layer. The next surgical repair was reported by Haight[5] in 1946. Here, a thoracotomy approach was used and this same approach has been used subsequently in all other patients reported in the literature.[3,5,7,10,12,13] By 1956 Koch and Clark[6] could find reports of only 16 patients corrected surgically.

The first recognized patient with an H-type tracheoesophageal fistula encountered in the Los Angeles Children's Hospital was diagnosed in April of 1954. Since then, two other patients were diagnosed in 1957. One hundred eight patients with fistulae and atresia of the esophagus had been operated upon in the same hospital by 1957. Our experiences with these three patients have been very helpful in providing knowledge of this important anomaly.

REPORT OF CASES

CASE 1. M.T. (reported in complete detail by Koch and Clark[6]) was admitted at two days of age on December 12, 1953, because of choking, regurgitation, and cyanosis with feedings since birth. Passage of a gastric tube ruled out esophageal atresia with a tracheoesophageal fistula. Roentgenographic examination revealed an aspiration pneumonia. Lipiodol passed through the esophagus without obstruction, and cardio-esophegeal relaxation (chalasia) was demonstrated. Some of the lipiodol entered the pharynx and tracheobronchial tree, but was thought to be due to regurgitation. Feedings of thick cereal were successfully retained and the patient discharged. During the next two months three more admissions followed for aspiration pneumonia. A history of occasional episodes of choking and cyanosis associated with feedings was obtained. Occasionally great abdominal distention was noted concurrently. On the last admission, iodized oil (2 to 3 cc) was introduced through a rubber catheter into the midportion of the esophagus with the patient in the prone position. Fluoroscopy and spot films revealed a fistula curving upwards from the esophagus to the trachea in a "tea-pot spout" configuration (Fig. 1). The grooving of an aberrant right subclavian artery was also demonstrated. Endoscopy failed to reveal the fistula but an inverted "V"-like fold of esophageal mucosa was noted on the anterior wall 11 cm from the upper alveolar ridge. No air bubbling was seen. Surgery through a posterior thoracotomy approach at the level of the third, fourth and fifth ribs revealed the

Fig. 1.—Iodized oil introduced into esophagus by catheter demonstrates "tea-pot spout" fistula high into trachea.

fistula to be very high in the neck. The tract was divided and both ends sutured. Two days postoperatively the infant died from sudden circulatory collapse. Autopsy revealed the esophageal opening to be 1 cm below the tracheal opening which was just 2 cm below the larynx. The esophageal opening was in the apex of the inverted "V"-like fold of the esophageal mucosa seen on esophagoscopy. The fistula was only 3 mm in diameter on entering the trachea.

CASE 2. D.McH. was admitted at three days of age because of vomiting and aspiration with her first feedings. A gastric tube was passed easily. With each feeding the infant immediately coughed, gagged and became cyanotic. Gastric distention was noted to increase with crying. Stools were frothy with air. Esophagrams, bronchos-

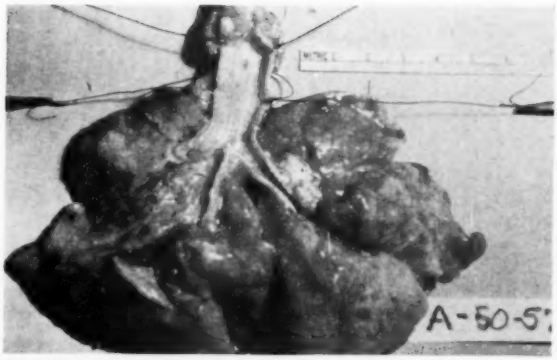

Fig. 2.—Opening of fistula into posterior wall of trachea just below larynx.

copy and esophagoscopy (utilizing Herweg and Ogura's[7] technique of instilling methylene blue into the trachea) failed to demonstrate the fistula. The swallowing function was irregular however, and slight aspiration of contrast media was noted. Paroxysms of coughing and dyspnoea continued with feedings. Repeated esophagrams with aqueous and oil contrast media failed to demonstrate a fistula. Two weeks later an exploratory thoracotomy failed to reveal a fistula in the thoracic esophagus. The infant expired four days later. Autopsy revealed an H-type fistula with the tracheal opening just 1.5 cm below the vocal cords at the level of the lower pole of the thyroid gland (Figs. 2 and 3).

CASE 3. D.McD. was admitted at three days of age because of choking and cyanosis with feedings since birth. A catheter had been passed into the stomach with ease. Esophagrams, laryngoscopy and upper esophagoscopy were all negative for evidence of a fistula. However, a repeat x-ray examination three days later using Hypaque swallows with the infant lying on his right side demonstrated a fistulous communication between the cervical esophagus and trachea 1.5 cm above the level of the first rib. This fistula was 0.5 cm in length and had the same "tea-pot" spout pattern seen in the first patient (Fig. 4). The following day a longitudinal incision in the left side of the neck through the platysma was made anterior to the sternocleidomastoid muscle. The carotid sheath was retracted laterally. The omohyoid muscle and thyroid gland were retracted medially and the esophagus and trachea exposed. The fistula was first

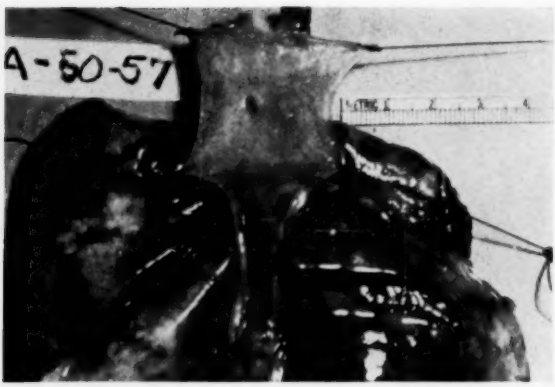

Fig. 3.—Larger, lower opening of fistula in anterior wall of esophagus in same patient.

searched for at the sternoclavicular joint level but found higher up at the level of the lower pole of the thyroid gland. It was ligated at each end and cut. Recovery was uneventful and the infant was discharged on the 19th postoperative day.

COMMENT

Symptoms. All three of these patients exhibited the classical triad of symptoms mentioned by most observers, that is: 1) paroxysmal attacks of choking, coughing and cyanosis with feedings. These are always greatest with liquids. Often the same patients can take semisolids without difficulty. Placing the patient in a prone position after feedings will sometimes initiate these symptoms or aggravate them. 2) Abnormal distention of the abdomen from increased amounts of air in the stomach and intestines because of the direct communication from the tracheobronchial tree into the esophagus. This is usually greatest and often dramatic when these patients cry or become choked with their feedings. 3) Recurrent aspiration pneumonitis. This constitutes the greatest threat to the patient's life and is the most frequent cause of death if the condition is undiagnosed. In addition to these symptoms one patient exhibited another finding suggestive of this condition. This was the passage of very frothy stools. Some writers believe that there is an increased amount of pharyngeal mucus but not as much as in those patients who have an

atresia of the esophagus. This was not noted in the cases reported herein.

Diagnosis. The above symptoms usually cause the physician to suspect an esophageal atresia with an associated tracheoesophageal fistula. This condition is quickly ruled out by the passage of a gastric feeding tube into the stomach. This is the point at which the mistake is often made in not appreciating that there may be a tracheoesophageal fistula without atresia or any other pathology of the esophagus. The next step in making a diagnosis is the use of fluoroscopy with a contrast swallow in the esophagus. In very few cases will this readily demonstrate a fistula. In our three patients a fistula was not demonstrated upon the first examination but the medium sooner or later appeared in the tracheobronchial tree. It is natural to assume that this is due to esophageal regurgitation, and then aspiration. However, if the examining fluoroscopist is satisfied that regurgitation and aspiration did not take place, this would be strong presumptive evidence of an H-type fistula. Usually, special techniques and procedures are necessary. Placing the patient in the prone position while the contrast medium is being introduced by catheter into the esophagus is advised and was successfully used in our first patient. In one of our patients (the third) the usual contrast swallow was unsuccessful but when Hypaque swallow was given with the patient on his righ side the fistula was demonstrated. The selection of the contrast medium should be varied if a fistula is not demonstrated initially. Some fistulae have been demonstrated with the initial use of an iodized oil. Others have not been demonstrated until thinner aqueous material was used. One of our cases was demonstrated using an oily medium after an aqueous solution had failed while in another an aqueous medium revealed a fistula that failed to show up with the use of iodized oil. At the present time our roentgenologist prefers the use of an aqueous medium as Urokon or Hypaque as these do not cause a chemical or aspiration pneumonitis and quickly disappear from the tracheobronchial tree. Placing the infant on his right side allows the fluoroscopist to visualize the area between the esophagus and trachea without one being superimposed upon the other.

Endoscopy. Esophagoscopy and tracheoscopy have failed to demonstrate the fistulae in our patients. In the first patient esophagoscopy did reveal the inverted "V" fold of the mucosa in the apex of which autopsy was to later reveal the fistulous opening. It is interesting that a similar fold of mucosa was described in one other patient by Pryles and Huvos.[8] In the second patient esophagoscopy and tracheoscopy again failed as did repeat procedures utilizing the

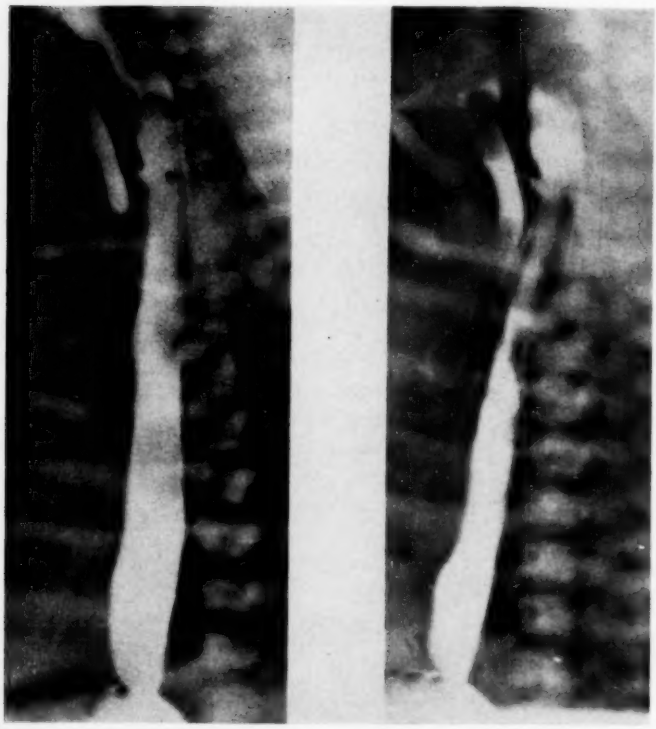

Fig. 4.—Aqueous medium swallow with infant in right lateral prone position demonstrates fistula similar to one in the Figure 1.

instillation of methylene blue into the esophagus by catheter and watching for its appearance in the trachea. In this case the technique of Herweg and Ogura[7] in which methylene blue was instilled by catheter into the uppermost trachea through an endotracheal tube while its appearance was watched for by esophagoscopy also failed. In both of our first two patients, and especially in the second, autopsy demonstrated that the fistulae were so high that the failure of tracheoscopy to demonstrate them was understandable. The tracheal orifices were so near the larynx that the true cords and conus elasticus overhung them in such a way that only extreme angulated inspection of the immediate subglottic area would have demonstrated them. In the third patient early x-ray demonstration of the fistula and the

indicated surgery prevented a second attempt to identify the fistula by endoscopy after its existence was known. Repeated endoscopy should be done, though, on all whether demonstrated or not by x-ray, as in this way can the exact level of the fistula be determined best. This is most important in the selection of the approach for surgical correction.

SURGERY

It was noted in the literature reviewed that the surgical approach was by a thoracotomy route in every instance except the case in which Imperatori used a transtracheal approach. Our first two patients had been explored transthoracically. In the first instance the fistula was found very high. In the second instance the fistula was so high that the exploratory thoracotomy failed to reveal it. Similarly, the x-ray examination revealed the fistula in the third patient to be very high in the cervical portion of the esophagus. Because of this the thoracic surgeon decided to use a superior mediastinal approach through the lateral neck (Fig. 5). This was eminently successful and was quickly performed with little difficulty. This, then, seems to be the first use of this route in the surgical repair of an H-type tracheoesophageal fistula. Convalescence from this surgical procedure should be much shorter and less stormy than that following thoracotomy. Many of the cases reported in the literature seemed to indicate that the fistula is often highly placed.[4,6-8,10,11] Our experiences would seem to indicate that the cervical approach should be considered first unless x-ray examination definitely locates the fistula in the chest. A fistula as low as 1 to 2 cm below the suprasternal notch could probably be repaired by this approach.[9]

Babbitt[10] reports a patient with two H-type fistulae. Bronchoscopy demonstrated one in the lower third of the trachea. This was corrected surgically. Autopsy a few days later revealed a second tracheoesophageal fistula just below the larynx.

Differential Diagnosis. In addition to tracheoesophageal fistulae with associated atresia of the esophagus, a number of other conditions must be considered. H-type fistulae have been searched for in newborn or very young patients who were later found to have such pathology as relaxed cricopharyngeus musculature, Reilly-Day syndrome, amyotonia congenita, chalasia, cardiospasm and various unusual spasm and dysfunctions of the esophagus.

Acquired Tracheoesophageal Fistulas. Three of the 108 patients who had surgical repair of fistulae associated with atresia of the esoph-

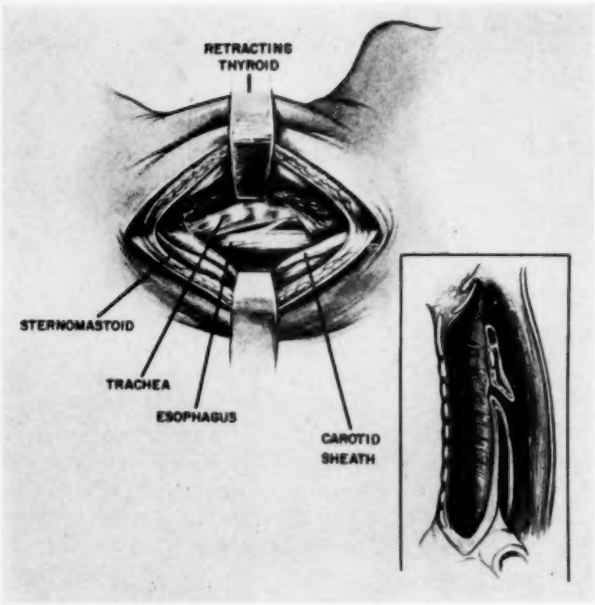

Fig. 5.—Cervical superior mediastinal approach for surgical repair of H-type tracheoesophageal fistula.

agus developed recurrent tracheoesophageal fistulae. These were equally difficult to demonstrate by endoscopy and radiological procedures. In one a definite blast of air up the esophagoscope with expiration was thought to have been helpful in making the diagnosis, later confirmed by re-operation. If recurrent aspiration pneumonia follows repair, the same repeated searches must be made.

SUMMARY

Experiences at the Los Angeles Children's Hospital with three patients with H-type tracheoesophageal fistulae lead to stressing the following points:

1. This type of tracheoesophageal fistula must be suspected in all infants who have repeated sudden choking and cyanosis upon taking feedings.

2. The triad of symptoms of a) choking and cyanosis upon feedings, b) distention of the abdomen, c) recurrent aspiration pneumonitis are constant findings in this condition. A very helpful additional finding is that of frothy stools which would seem to be very suggestive of this anomaly.

3. The presence of such a fistula is best demonstrated by repeated use of contrast media placed in the esophagus by swallow or with a catheter and with the patient in the right lateral prone position. Aqueous media are preferred because of their lower viscosity. If oil media fail to reveal the fistula, aqueous solutions should be used. Repetition of examinations in various positions and with varying media is probably most important.

4. If endoscopy at first fails to reveal the orifices of a fistula special attention should be given to the immediate subglottic area of the trachea. Angulation of the endoscope and the use of telescopes may help in demonstrating the fistula's orifice. The presence of abnormal folds of mucosa of the anterior wall of the upper esophagus should arouse suspicion that such folds may hide a fistulous opening.

5. The opening of the anterior wall of the esophagus is usually situated lower and is more widely open than is the orifice into the posterior wall of the trachea. This often results in the typical "teapot spout" configuration when the fistula is filled with a contrast medium.

6. If the fistula is very high its repair by the superior mediastinal approach should be considered first. The first such repair is noted.

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LXXXII

ENDOSCOPIC ASPECTS OF PRIMARY TUBERCULOSIS IN CHILDREN

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During the course of primary tuberculosis infection in children, dense, homogeneous shadows are frequently seen on x-ray films. Their appearance often seems to have little or no effect on the well-being of the child, even though segments or even whole lobes may be involved. After many months, the shadows clear leaving the lung without any evidence of disease. Eliasberg and Neuland[12] described these shadows and called attention to their benign clinical course. They concluded that the process was a nontuberculous consolidation and used the term "epituberculosis" to identify this clinical entity.

Their observations stimulated considerable interest in the nature of the process. From the extensive literature which has grown about this subject, two principal views have evolved: 1) that the shadows represent a resolving tuberculous pneumonia and 2) that the principal change is an atelectasis due to bronchial obstruction. Rich,[35] after reviewing the clinical, pathological and experimental evidence supporting these two views, concluded that neither should be held to the exclusion of the other. However, in recent years the role of bronchial obstruction and atelectasis has become more firmly established as the principal factor in producing these shadows. Bronchoscopic observation of changes in the tracheobronchial tree during primary tuberculosis has contributed substantially to our understanding of this process. Indeed, bronchoscopy has become the most rewarding diagnostic procedure in the management of primary tuberculosis.

In 1947 a combined clinical and bronchoscopic study was started by the Children's Chest Service and the Department of Otolaryngology of Bellevue Hospital. The objectives of the investigation were:

1. To study the bronchial changes in primary tuberculosis by repeated bronchoscopic examinations and thus, from a large number

of observations, to determine the evolution of the endobronchial lesion.

2. To assess the role played by the endobronchial lesion in producing pulmonary changes such as consolidation, atelectasis and emphysema.

3. To determine the permanent effects of endobronchial lesions a) on the bronchial wall and b) on the parenchyma of the segments or lobes involved, i.e., their role in producing bronchiectasis, compression or crowding and fibrosis.

4. To evaluate local bronchoscopic therapy such as aspiration and removal of tuberculous granulomas on the course of the disease.

5. To evaluate the effect of antituberculous drugs on the endobronchial lesion.

The population studied was the children admitted to the Pediatric Chest Service of Bellevue Hospital under Dr. Edith Lincoln's direction. Not all of the patients admitted to the service during this time were bronchoscoped; only those whose clinical course and x-ray findings suggested endobronchial involvement or segmental obstruction were included in the study. The present report is the result of an analysis of the findings of 156 patients with proved tuberculous endobronchitis. This is a selected group and does not include every child with tuberculous bronchitis, since some cases may have gone undetected.

PATHOGENESIS OF PRIMARY TUBERCULOUS ENDOBRONCHITIS

The pathogenesis of primary tuberculous endobronchitis is important for understanding the clinical problem of endobronchial tuberculosis. The tubercle bacilli inhaled by the infant or child reach the alveoli in the periphery of the lung usually in the lower part of the lobes. Multiplication of organisms produces a ocal, acute inflammatory reaction, the severity of the reaction depending upon the number of bacilli present. The bacilli are engulfed by monocytes and are carried along by the flow of lymph to the first lymph nodes located at the origin of the segmental bronchus. The primary focus, the involved intrapulmonary lymph node and the intervening lymphatics comprise the primary complex. Beyond this point, they are carried to the next echelon of nodes, the hilar and mediastinal group, where conditions for their multiplication seem ideal.

The first response of the tissue to the presence of the tubercle bacilli is an acute inflammatory reaction. Within a short time, however, the body becomes sensitized to the tuberculoprotein and an allergic reaction takes place locally in the parenchyma of the lung and in the involved lymph nodes. The period of latency between the start of infection and the onset of hypersensitivity varies from three to twelve weeks. Clinically, the beginning of the allergic reaction is marked by the development of skin hypersensitivity to tuberculin and roentgenographically, by the appearance of shadows at the primary site and marked enlargement of the hilar lymph nodes.

Thus, in primary tuberculosis the enlargement of the lymph nodes is always present and is so common a feature that it dominates the clinical picture. This has influenced some observers to consider primary tuberculosis to be essentially an infection of the lymphatic system. As the nodes enlarge the capsule becomes involved in the inflammatory reaction and adheres to the surrounding structures.

Because of the location of the lymph nodes along the trachea and bronchi, these structures are most frequently involved by the process. However, there are other possible ways in which a bronchus may develop an endobronchial lesion. The initial focus of infection may be in the bronchial or tracheal wall; this would be a true primary or chancre as described by the French authors. We have not seen any such case. Mounier-Kuhn has reported one in his series. The difficulty lies in establishing the validity of the case: one must exclude the possibility of the presence of an overlooked primary in the lung. The fact that such a primary chancre of the bronchus occurs so infrequently, if at all, is undoubtedly an indication of the efficiency of the protecting layer of mucus and ciliary activity of the bronchial mucosa. The absence of this protection may explain why the tubercle bacilli becomes localized in the alveoli.

Another method of infection is the involvement of the bronchi by the tuberculous lymphangitis of the peribronchial lymphatic vessels draining a primary lesion.

PATHOLOGY OF ENDOBRONCHIAL TUBERCULOSIS

As the infected nodes enlarge, they fix the adjacent bronchus and compress it. The soft wall of an infant's bronchus is easily compressed; the lumen becomes narrow and slit-like. The advancing inflammatory reaction from the capsule of the gland extends through

all the layers of the bronchus. It reaches the mucosa producing a localized congestion and edema, giving the involved area a characteristic velvety appearance. Further progression produces a necrosis of the epithelial layer and a typical ulceration is formed. Tuberculous granulation tissue forms at the base of the ulceration. This may become exuberunt and form a definite polyp of tuberculous granulation tissue, which projects into the lumen partially or completely obstructing it. The process may stop and gradually heal; or the continued pressure of a caseous node may cause necrosis of the wall and the caseous material from the node may escape into the bronchus. In this way a fistula is formed between the node and the bronchus.

The pathological changes in the bronchi cause definite changes in the segment of the lung to which it is distributed. In some instances, either by compression or the presence of a polyp, a check valve mechanism is set up and the segment, lobe or even entire lung may become emphysematous. The obstruction usually becomes complete and atelectasis results. In the roentgenogram, the atelectatic segment may appear as a homogeneous shadow, typical of airless lung tissue diminished in volume. Frequently the lobe or segment does not decrease in volume. This is due to distention by retained secretions. The ulceration of the mucosa stops ciliary activity and the peribronchial inflammation prevents contraction of the bronchus; thus, the two mechanisms for moving secretions out of the bronchus are interfered with.

The bronchi heal by fibrosis which, in the final stages, causes stenosis, distortion and dilatation, i.e., bronchiectasis. Fibrosis may extend through the parenchyma of the segment reducing it to a nonfunctioning, crowded unit.

Since the pathological changes in the tracheobronchial tree and the parenchyma of the lung are secondary to nodal involvement, it is evident that the anatomical location of the nodes will determine the pattern of the disease process.

The typical location of lymph nodes at the point of division of the bronchi explains the frequent occurrence of endobronchial lesions at or just above a bronchial orifice.

CLINICAL PICTURE

Primary tuberculosis in children is, in the majority of instances, not a serious disease, either from the standpoint of morbidity or

TABLE I

DISTRIBUTION OF 156 CHILDREN WITH TUBERCULOUS ENDOBRONCHITIS BY AGE AND SYMPTOMS

AGE	TOTAL NUMBER	WITH DEFINITE SYMPTOMS	
		NUMBER	PER CENT
6 months	10	9	90
6-11 months	29	18	62
1-2 years	72	26	36
3-4 years	25	4	16
5 years	20	1	5
TOTAL	156	58	37

mortality. A good many primary infections go undetected clinically. The mortality rate in nearly one thousand children hospitalized for primary tuberculosis at Bellevue in the years 1940 through 1946 was slightly over 20 per cent. This was prior to antimicrobial therapy. Ninety-five per cent of the deaths were caused by meningitis, miliary tuberculosis and more protracted forms of hemotogenous tuberculosis, or locally progressive primary tuberculosis with evidence of cavitation and bronchogenic spread. The development of endobronchial tuberculosis was not considered a serious complication and was the direct cause of death in only one case. Since the advent of antituberculous drugs, the mortality rate has dropped due to control of the serious complications but the incidence of endobronchial tuberculosis remains the same.

Cough is the most frequent symptom produced by the endobronchial lesions. It is a brassy, paroxysmal cough and is frequently accompanied by an audible wheeze. Severe symptoms, such as wheeze, dyspnea, cyanosis and marked spasmodic cough are more common in infants and young children than in older children. The more severe symptoms in the infant and younger child are explained by the fact that the bronchi are smaller and more easily compressible. For the same reason endobronchial tuberculosis has a more serious prognosis in the infant. The most common physical findings are diminished breath sounds, dullness and a persistent wheeze usually located on one side.

LABORATORY EVIDENCE

All patients had three gastric lavages soon after admission and thereafter at least once every month while in the hospital. Cultures of bronchial fluids were obtained at each bronchoscopic examination. A comparison of these two methods of obtaining cultures is made in Table II. The higher percentage of positive cultures was obtained by gastric lavages. It should be noted that the bronchial secretions were positive in eight cases in which gastric fluids were persistently negative.

TABLE II

ONE HUNDRED AND FIFTY-SIX PATIENTS WITH TUBERCULOUS ENDOBRONCHITIS; CULTURES FOR TUBERCLE BACILLI FROM GASTRIC AND BRONCHIAL FLUIDS

POSITIVE GF* NEGATIVE BF**	NEGATIVE GF POSITIVE BF	POSITIVE GF POSITIVE BF	NEGATIVE GF NEGATIVE BF		
59	8	37	52		
Patients with Positive Cultures				104	66.7%
Patients with Positive GF Cultures				96	61.5%
Patients with Positive BF Cultures				45	28.1%

* GF - gastric fluid

** BF - bronchial fluid

ROENTGENOGRAPHIC EVIDENCE OF BRONCHIAL OBSTRUCTION

Dense, homogeneous shadows indicating bronchial obstruction of a segment or lobe were present in all but 15 of the 156 patients in the study. The shadows persisted for variable lengths of time from weeks to several months. Clearing was usually gradual. In a few instances, shadows would appear and disappear within a period of a few days. This was considered to be due to intermittent obstruction.

Roentgenographic evidence of obsruction was found more often in the right lung. The middle lobe and the anterior segment of the right upper lobe were the most common sites of obstruction. On the left side the lingular lobe was most often involved.

TABLE III

ROENTGENOGRAPHIC EVIDENCE OF BRONCHIAL OBSTRUCTION

Limited to one or more segments of one lobe		110
Two or more lobes		27
Entire lung	2	
Bilateral	7	
Emphysema only		4
No evidence		15
Total		156

Localization of obstruction according to segments is shown in Figure 1.

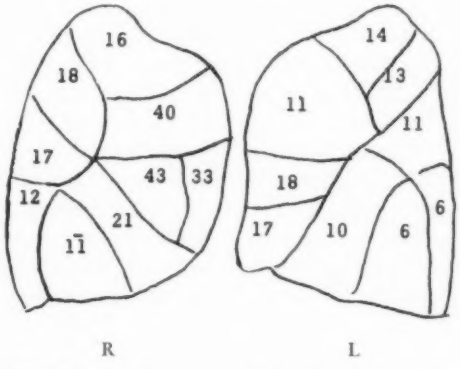

Fig. 1.—Distribution of segmental obstruction in 156 patients with tuberculous endobronchitis.

BRONCHOSCOPIC STUDY

General anesthesia was considered desirable because it permitted a more deliberate search for minimal changes in the tracheobronchial tree and also reduced the psychic trauma to the child. Various forms of anesthesia were tried. Surital, given rectally, was chosen as the

most suitable for the study. The dosage of surital was 1 gram per fifty pounds of body weight administered rectally in a 2 per cent solution. There were two difficulties with this form of anesthesia. One difficulty was the inability to predict the level of the drug in the circulating blood when absorbed from the rectum. This meant a variation in the amount of relaxation achieved; however, only 5 per cent of the cases were considered so unsatisfactory that the bronchoscopy could not be done. The second difficulty was the tendency to develop laryngospasm, bronchospasm and apnea, characteristics of all barbiturates. This was overcome by aerosolizing 8 cc of 0.5 per cent solution of pontocaine to which had been added epinephrine and a wetting agent, triton. This vapor was administered through a No. 41 De Vilbiss nebulizer to which a short piece of rubber tubing had been added. As the surital anesthesia deepened, the rubber tipped end of the vaporizer was advanced into the oral cavity and pharynx. By this method anesthesia of the tracheobronchial tree was accomplished and laryngospasm and bronchospasm eliminated. There were no reactions to the pontocaine. This was undoubtedly due to protection given by the surital. The contrast between the pale, anesthetized, normal mucous membrane and the congestion of the early lesion made identification easier. Suitable Jackson type bronchoscopes were used. A right angle telescope, small enough to pass through a No. 4 bronchoscope was helpful in visualizing the upper lobe bronchi. The entire tracheobronchial tree was inspected. Secretions for culture were collected and masses of granulation tissue, when accessible, were removed for pathological examination.

This technique has been used in over 1,200 bronchoscopies in children without any serious complications. Postbronchoscopic laryngeal edema has not been a problem. No tracheotomies were required. There was no evidence in this series that bronchoscopy had a deleterious effect on the course of the disease or caused a spread of infection.

BRONCHOSCOPIC APPEARANCE OF THE LESION

There were several types of lesions seen through the bronchoscope which were typical of the various stages in the development of the disease:

1. First or minimal lesion: fixation of the bronchi by a group of enlarged nodes takes place; the normal motility of the structures during respiration is reduced and passive movement with the bronchoscope elicits resistance. This occurs when the nodes of the bifurcation

and the right paratracheal group become enlarged and surround the right main bronchus, without compressing it; congestion of the bronchial mucosa is usually present.

2. Compression by an enlarged node: the bronchial lumen is reduced, often to a slit-like or lunar opening. It is not uncommon to find the segment or lobe emphysematous or atelectatic beyond the point of compression.

3. Mucosal congestion and edema: this is due to a localized inflammatory reaction in the bronchial mucosa, next to an enlarged node. The mucosal inflammation may also be caused by retrograde lymphangitis from an inflamed area. The lesion was most frequently seen at the orifice of the segmental bronchi or just above the opening of the right or left main bronchus.

4. Ulceration: in the next stage the surface epithelium is lost and a shallow ulcer forms. Many of the lesions do not advance beyond this point.

5. Granuloma: an exuberunt mass of tuberculous granulation tissue may grow from the ulcerated area. It is usually pedunculated and has the appearance of a polyp. Its surface is flecked with caseous material. Granulations may be present at the point of rupture of a node and may spring simultaneously from several areas indicating involvement by several nodes. Thus, nodes of the bifurcation may produce granulomas in both the right and left main bronchus simultaneously.

6. Fistula formation: the continued pressure and inflammation of a caseous node on the bronchial wall produces necrosis. The weakened point in the bronchial wall permits the escape of caseous material from the node. The rupture may come suddenly and the gland empty its contents into the trachea. Large formed masses may obstruct the airway and produce sudden asphyxia. This type of rupture is very rare, occurring only once in the rather large experience at Bellevue. Usually the material is slowly extruded. In several instances the caseous material could be expressed by making pressure on the wall above the fistula with the beak of the bronchoscope. In others, an aspirating cannula was introduced into the opening and caseous material was removed. The opening of the fistula may appear as a necrotic hole in the bronchus or it may be surrounded by granulations.

7. Stenosis: scarring in a bronchus may produce a stenosis of varying degrees. In one instance, the left main bronchus was reduced to a 2 mm opening. It was not uncommon to observe a middle lobe bronchus become completely stenotic after a severe ulceration of a bronchus. In Table IV the incidence of bronchoscopic findings is recorded.

TABLE IV

BRONCHOSCOPIC FINDINGS IN 156 PATIENTS

Narrowing of lumen due to external compression		36
Narrowing of lumen due to disease within bronchus		42
Stenosis of bronchus		10
Granulation tissue		114
Polyps	54	
Ulceration of bronchial wall		20
Caseous material within bronchus		50
Erosion of bronchial wall		25

The findings presented in Table IV represent the total count of each type of abnormality and a single case may be represented in more than one category. Erosion of the bronchial wall was included only if an actual break was seen in the mucosa or if caseous material was observed extruding from the bronchial wall.

One of the early objectives of the study was to determine the duration of endobronchial involvement in the group by measuring the interval between the first diagnostic bronchoscopy and healing. The plan was to do a bronchoscopy at least every three months until an end point was reached. Because of unavoidable delays between bronchoscopies, it was not possible to calculate the duration of active disease in all patients; it was done in only 70 children and the results are shown in Table V.

In two-thirds of the cases the endobronchial lesion lasted one year or less; one-third persisted for over a year.

The investigators believe that there was no definite beneficial effect of antimicrobial therapy on the endobronchial lesion in this group. Forty of the 70 patients received antimicrobial therapy for

TABLE V

DURATION OF ACTIVE ENDOBRONCHITIS BY BRONCHOSCOPY IN 70 PATIENTS
Relation to Specific Therapy

DURATION OF ENDOBRONCHIAL INVOLVEMENT	NO. OF PATIENTS	DURATION OF SPECIFIC THERAPY			
		NONE	LESS THAN 6 MONTHS	6-11 MONTHS	OVER 1 YEAR
Less than 3 months	11	4	0	5	2
6-11 months	36	3	12	10	11
More than 1 year	23	3	8	2	10
Total	70	10	20	17	23

six months or more, yet in 33 of these patients active endobronchitis continued to be observed bronchoscopically for a period ranging from six months after treatment was begun to more than three years.

BRONCHOGRAPHIC STUDY

The observation that the homogeneous shadows which persisted for months eventually cleared, led early observers to believe that the lung was normal. However, in 1932 Brock drew attention to the fact that no one had demonstrated that bronchiectasis developed in these collapsed segments.

To provide the answer to this problem, Kent in 1942 did bronchograms on ten patients who had had collapsed segments that cleared; seven out of ten had bronchiectasis.

In order to determine the incidence of permanent damage to the bronchi and parenchyma, the children in our series were studied clinically, also by x-ray and bronchography. Clinical examination alone was not helpful in assessing permanent damage, since children with bronchiectasis secondary to tuberculous endobronchitis rarely present the clinical picture of suppurative pulmonary disease. They are usually symptom free. On plain films, thirty-one, or about 20 per cent of the entire group of 156 patients had roentgenographic evidence of one or more contracted pulmonary segments. As would be expected, bronchograms gave the best evidence of damage to the

bronchi. Bronchograms were obtained without selection in 103 of the 156 cases. Results are shown in Table VI.

TABLE VI

BRONCHOGRAPHIC FINDINGS IN 103 PATIENTS

Normal			33
Abnormal			70
Minimal Abnormalities		20	
Crowding of bronchi	6		
Narrowing of bronchi	4		
Cylindrical bronchiectasis	9		
Saccular bronchiectasis	1		
Marked Abnormalities		50	
Crowding of bronchi	5		
Stenosis of bronchi	10*		
Cylindrical bronchiectasis	29**		
Saccular bronchiectasis	6***		
Total			103

* One of these showed bronchiectasis in resected lobe.
** One additional case showed bronchiectasis in resected lobe.
*** One additional case showed bronchiectasis in resected lobe.

In the group with minimal abnormalities, the dilatation of the bronchi was either slight in extent or localized to a very small area. The bronchial narrowing was never more than 50 per cent.

Among the 103 children with endobronchial tuberculosis, bronchograms were normal in 33 children or 32 per cent and abnormal for 70 children, or 68 per cent.

EFFECT OF ANTIMICROBIAL THERAPY IN ENDOBRONCHIAL TUBERCULOSIS

The prognosis of primary pulmonary tuberculosis has been greatly altered by antimicrobial therapy. In the Chest Clinic of the

Children's Medical Service of Bellevue Hospital, the death rate from primary tuberculosis was only 1 per cent in the years 1952 through 1954, as compared with a mortality of 21.5 per cent before the advent of antituberculous drugs. The marked drop in mortality is due to control of the serious complications such as meningitis, the miliary form and the progressive primary. In contrast, endobronchial tuberculosis has not responded as strikingly to antimicrobial therapy. In this failure to respond to therapy it is interesting to compare the childhood form with the adult type of tuberculous endobronchial lesions. Endobronchial disease in adults is due to the bathing of the mucous membrane lining a bronchus with sputum containing tubercle bacilli, usually derived from an adjacent cavity. The ulceration begins in the mucosa and heals rapidly under antimicrobial therapy. Moreover, the source of the infection in the cavity is simultaneously controlled by specific therapy so that relapse or reinfection of the bronchial mucosa is prevented. In the children, the caseous node produces the lesion. Two factors account for the lack of response: 1) the large amount of caseous material, under pressure, prevents the antimicrobial agent from reaching the organisms and 2) although the caseous materal may contain few living tubercle bacilli, there is enough tuberculoprotein to produce a typical reaction in the bronchial wall. In a few cases which were treated intensively for meningitis or an extrapulmonary focus, we observed endobronchial disease develop and progress through all phases from compression to rupture of the caseous node into a bronchus. Thus, while a favorable response occurred in the extrapulmonary lesion, the bronchial lesion was unaffected.

During the period of the study there were many instances of variation in the antimicrobial therapy both as to agent, quantity and combination of agents and duration of therapy. We have not attempted to analyze results according to various schemes of therapy, but have included in the treated group all children who received six weeks or more of daily antimicrobial therapy with streptomycin or isoniazid.

Using the duration of the endobronchial lesion observed bronchoscopically as the standard, there was no evidence that antimicrobial therapy exerted a rapid, beneficial effect on endobronchial disease. Nor is there any evidence of reduction in the incidence of bronchiectasis in the obstructed lobes of children who received antimicrobial therapy. There was no significant difference in the incidence of bronchiectasis in the treated and untreated groups or in the group treated for less than six months and the group treated for more than six months.

TABLE VII

RELATIONSHIP OF BRONCHOGRAPHIC CHANGES TO SPECIFIC THERAPY

	TOTAL		UNTREATED		TREATED LESS THAN 6 MONTHS		TREATED MORE THAN 6 MONTHS	
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Normal bronchograms	33	32.0	6	28.6	11	34.4	16	32.0
Abnormal bronchograms	70	68.0	15	71.4	21	65.6	34	68.0

Thus, in this group of cases there was no striking evidence that specific therapy prevented secondary damages to the lungs or bronchi in patients with tuberculous endobronchitis.

SURGERY IN TREATMENT OF ENDOBRONCHIAL TUBERCULOSIS

Surgery was used to remove lung segments showing irreversible changes. Ten children have had surgical resections of diseased pulmonary tissue. The decision was made individually based on the following indications:

1. Extensive areas of bronchiectasis, especially in the middle and lower lobes. It was felt that these would be more susceptible to secondary infection in adult life.

2. Airless segments.

3. Marked narrowing or complete stenosis of a bronchus, especially when it involves a major bronchus.

4. Segments containing a large amount of calcium within an obstructed area. These areas, when resected, usually contain caseation and active tuberculosis which might become reactivated in adult life.

Other workers have made a direct surgical attack on the enlarged nodes, removing them and repairing the bronchial fistulae when present. Direct surgical attack on the diseased nodes was not done in any of our cases.

CONCLUSIONS

1. Bronchoscopy plays an important part in the management of primary tuberculosis.

2. Medical treatment with antituberculous drugs has failed to alter the course of the endobronchial lesion or to prevent development of bronchiectasis and pulmonary fibrosis. Even though this is true, it should not be withheld, as there is every reason to believe that it diminishes the dangers of bronchogenic spread.

3. Search for new drugs and new regimes of treatment aimed at controlling the endobronchial lesion and preventing its sequelae, should be continued. At the present stage of our study a combination of antituberculous and steroid drugs, e.g., isoniazid and para-aminosalicylic acid, is being used. The results have been very encouraging. The lesion disappears within a few weeks; however, if therapy is discontinued the lesion rapidly returns. Prolonged therapy with steroids and antituberculous drugs holds out great promise of controlling primary endobronchial tuberculosis and preventing its sequelae.

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LXXXIII

MASSIVE ATELECTASIS IN BRONCHIAL ASTHMA

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Bronchial asthma is a common form of acute or chronic bronchial inflammation usually of allergic origin. It is present in 2 to 5 per cent of the whole population of the United States with the incidence in children roughly the same.

Patchy transient atelectasis is a frequent complication of chronic asthma;[12] however, massive pulmonary collapse as a complication of asthma is a very rare condition. Only 12 documented cases of nontraumatic and nonoperative massive atelectasis are found in the English language literature.[3,4,6,7,9-15] The purpose of this paper is to present another case and review the literature of this uncommon sequela of asthma.

REPORT OF A CASE

E.W., a 10½ year old white female, was admitted to the UCLA Hospital on December 12, 1957, with a history of difficult breathing and left chest pain of 48 hours' duration. There was a history of bronchial asthma since the age of 18 months, which was not severe. The patient had been treated with bronchodilator inhalant during the last six months and had little difficulty. She did not require epinephrine injections. Two days prior to admission she developed a sore throat, unproductive cough, dyspnea and pain across the anterior and posterior chest walls. She vomited a small amount after the onset of chest pain. There was no recent wheezing and no history of foreign body aspiration.

Physical Examination. Physical examination revealed a well-developed, and well-nourished white female child in moderate respiratory distress. Temperature was 37.9 C, pulse 140 and respirations 48. The pharynx and tonsillar pillars showed moderate erythema. She

appeared to have slight pain in the mid-back with flexion of the neck, and did not have normal flexibility of the back. The left chest was flat, with decreased motion on inspiration. The breath sounds were decreased on the left, especially at the base, with decreased fremitus on that side. No wheezes were heard. There was marked dullness over the left rib cage below the level of the scapular spine. The PMI of the heart was in the anterior axillary line and the area of cardiac dullness was shifted to the left, with the right cardiac border to the left of the sternum. The heart sounds were normal. The remainder of the examination was within normal limits.

Laboratory Data. The hemoglobin was 16.6 gm per cent, hematocrit 48 per cent, white blood cell count 9,950 and sedimentation rate 15 mm/hour (Wintrobe). Nasopharyngeal and throat cultures showed mixed non-pathogens, except for some beta streptococci in the throat. X-ray of the chest revealed atelectasis of the left lower lobe and lingular segment of the left upper lobe. There was a shift of the mediastinum to the left and herniation of the right lung into the left side (Fig. 1).

Hospital Course. It was concluded that the patient had a mucus plug in the left main bronchus. Attempts to remove the plug by pounding on the chest with coughing, postural drainage and by the use of the positive pressure Bennett machine intermittently were unsuccessful. An attempt to insert an endotracheal catheter for suction was unsuccessful. Bronchoscopy was performed under ether anesthesia on the day of admission. Thick, tenacious mucus was found filling the left main stem bronchus. This was aspirated and collected for culture. The left bronchial tree was inspected and no evidence of foreign body was found. More thick mucus was obtained from the left lower lobe. Neo-synephrine® solution, ¼ per cent, was instilled into the left main stem bronchus and then aspirated. This was followed with 5 cc of acqueous Tryptar.® Immediately following bronchoscopy there was a marked increase in the excursion of the rib cage on the left, shift of the heart to the normal position and increased breath sounds on the left. The breath sounds did not reach normal intensity for several hours and there continued to be rales, rhonchi and expiratory wheezes until discharge. Upon recovery from anesthesia, chest pain and dyspnea were relieved and she was able to clear her bronchial tree by coughing up clear thick mucus. X-rays 12 hours postoperatively showed the mediastinum shifted back into the normal position with a small area of atelectasis in the lingular segment of the left upper lobe and a small amount of fluid in the left pleural space (Fig. 2). Culture of the bronchial washings revealed alpha streptococci predominating, with a few gamma streptococci

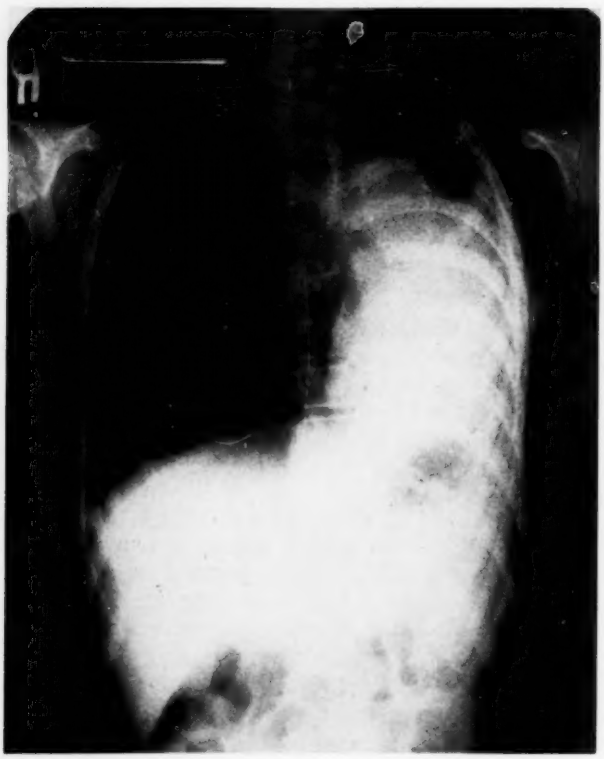

Fig. 1.—Atelectasis of left lower lobe and lingular segment of left upper lobe with shift of the mediastinum to the left side.

and a few coagulase positive micrococcus pyogenes aureus, sensitive to all antibiotics. Postoperatively, the patient received penicillin and saturated potassium iodide solution combined with postural drainage. She was discharged asymptomatic to her private physician on the third day after admission. Her chest film prior to discharge showed increased bronchovascular pattern in the left lung, especially in the lower lobe, but was otherwise normal.

COMMENT

Factors predisposing to bronchial obstruction in asthma are allergic edema of the walls of the smaller bronchi and bronchioles,

Fig. 2.—Postoperative film showing clearing of the atelectasis with shift of the mediastinum to the normal position.

spasm of the smooth muscle of the bronchial walls, and the secretion of a thick, tenacious mucus from the bronchial glands. This increased secretion of mucus leads to a concomitant decrease in ciliary action, thus promoting stasis of the secretion.[5] As narrowing of the airway progresses, the respiratory rate is increased with subsequent dehydration resulting from the loss of inexorable fluid during this increased respiratory activity. This causes the mucus to become inspissated, forming tenacious plugs that are capable of obstructing the bronchi.

It is uncommon in adults for a bronchus proximal to the segmental divisions to be occluded sufficiently by retained secretions to cause collapse unless the cough mechanism is impaired.[9] This occurs

following major surgical procedures, especially thoracic and abdominal operations, with ensuing pain and narcosis together with the impairment of ciliary activity and increased flow of mucus due to the direct effect of anesthetic agents on the bronchi.[8] In children and infants, however, the smaller caliber of the bronchi lend themselves to obstruction and collapse whenever bronchial pathology is present. Seven of the reported cases were in children with recurrent attacks in two. Of the five adult cases, the atelectasis in two was bilateral[3] resulting in death of the patients, although one was complicated by cardiac failure.[7] In both of these cases, the physical findings for massive atelectasis are not mentioned, nor is there radiological evidence presented confirming it, the condition being proved at autopsy. Nine cases gave a history of asthma, and two others, although not stated in the case reports, are assumed to have an asthma history as the atelectasis occurred during an asthmatic attack. The case cited by Peshkin and Fineman[11] concerns a nine year old boy with massive atelectasis of the left lung with no history of previous respiratory symptoms. Subsequent to this illness, the patient had recurrent asthma. The child, however, sustained trauma to his chest two days prior to his symptoms and this case could be considered postraumatic.

In one-half of the cases the atelectasis was precipitated by an asthmatic attack, while in the other six the symptoms preceding the collapse were not associated with clinical evidence of an asthmatic attack. The most constant symptoms in all cases were chest pain and cough. Six cases reported involvement of the left lung, while three showed the right lung affected. Rakower[13] cites a case of an eight year old boy having massive atelectasis during asthmatic attacks on four separate occasions, three times in the right and once in the left lung. The other two cases had bilateral involvement ending in death.

Treatment is primarily directed toward removing the obstruction within the bronchi. Antibiotics are used concurrently as prophylaxis against infection in the atelectatic lobes. If the atelectasis is not corrected by conservative measures within a relatively short period of time, bronchoscopy should be performed. The bronchoscopic findings are relatively constant, revealing a viscid, tenacious mucoid material with occasional inspissated plugs being seen. Aspiration of the secretions effects immediate re-expansion of the lung, with dramatic relief of symptoms. The instillation of digestive enzymes during the procedure facilitates the clearing of the bronchial tree as one of the immediate effects of trypsin is digestion of the mucus.[1,2] Seven of the cases were treated by bronchoscopy with immediate clinical improvement and complete clearing of the lungs within 1 to 7 days.

With conservative treatment, improvement occurred on the average within 3 to 5 days with clearing of the lungs within 1 to 4 weeks.

SUMMARY

Atelectasis may be termed massive when more than one lobe is involved. It is a rare complication of bronchial asthma, occurring more often in children and frequently heralded by symptoms not associated with bronchospasm. Massive unilateral pulmonary collapse is in itself not fatal, although the anoxia and increased cardiac labor that it produces may contribute to a fatal outcome. Several instances of resulting death are reported when the involvement was bilateral. The condition usually clears with conservative measures; however, bronchoscopy expedites recovery and prevents further complications. When available it is, in skilled hands, regarded as the best method of treatment.

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LXXXIV

BRONCHIAL ADENOMA IN CHILDHOOD

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Adenomatous lesions primary in large bronchi are generally held to be uncommon in the pediatric age group. No such case was reported to the New York Children's Tumor Registry in the first ten years of its existence, or until 1951.[18] However, at least 20 cases diagnosed before the age of 16 years (six before the age of ten) have been found in the literature. Seventeen of these are included in three recent brief reviews.[16,18,24] Several are presented only by passing reference in extensive reports of the general problem. An additional case, the first encountered at the Children's Medical Center in Boston, is reported here. One further example in this age group, diagnosed elsewhere, and as yet unreported, is known to us. Reference to this condition in children was made as early as 1926,[9] but the polyp removed was not described histologically. The youngest patient noted in the literature was four years old at the time of diagnosis.[2]

The problem assumes importance with reference to two additional impressions: the number of reported bronchial adenomas diagnosed between the ages of 16 and 20 years approximately equals those collected here. Many general reviews of these tumors describe one or more adults with histories of pulmonary invalidism dating back as long as 20 to 30 years. The apparent trend is to earlier diagnosis and may require revision of current ideas of average age of onset.

Adenoma of the bronchus was first recognized at post-mortem examination in 1882 by Mueller (quoted from Ward et al.[24]). According to Klein,[12] this tumor comprises 75 per cent of all benign bronchial tumors of any age, but the incidence of benign tumors of the bronchi or lungs is very low. In a series of 217 histologically proved primary lung tumors at the Lahey Clinic in Boston over an 18 year period, Souders and Kingsley[20] in 1948 reported that bron-

chial adenoma comprised only 6.9 per cent. Clerf and Bucher[3] in 1943 reported a 12 per cent incidence of adenoma in a series of 278 primary tumors diagnosed bronchoscopically at Jefferson Clinic in Philadelphia from 1927-1942. In a discussion at the annual meeting of the American Broncho-Esophagological Association in 1954, Overholt quoted a 4 per cent incidence in his clinic in Boston. At this same meeting Soutter[21] reviewed the Massachusetts General Hospital series of 56 bronchial adenomas from 1923 to 1954, and noted that 53 of the 56 were of the carcinoid (Jackson) type, and the other three were typical cylindromas. Forty-six were diagnosed by biopsy on the original bronchoscopy, indicating the importance of this procedure. Of the 53 patients with the carcinoid type, 32 had bronchiectasis, nine empyema, and four lung abscesses. Forty-one were still living, three unoperated upon. Two of the three patients with cylindromas were dead, as were 13 of those with the carcinoid type.

In general, the symptomatology, diagnosis, treatment, and prognosis of these tumors in childhood pose the same problems as does the condition in adults. The following clinical triad may be of value in suggesting this disease:

1. Hemoptysis, often sudden, is frequently the first symptom noted. Unless associated with long-standing bronchiectasis, there is usually pure blood, and bleeding may be profuse. Only about one-third of the cases reported in children manifested hemoptysis.

2. Recurrent pneumonitis and chronic cough are the commonest complaints. The cough at first is dry and irritative, and later becomes looser and worse at night. The sputum becomes thicker, more profuse and more purulent as the bronchial obstruction increases, and secondary infection develops. The pneumonitis is unilateral and may rarely be migratory on the involved side.

3. Bronchial occlusion is noted by physical signs or roentgenographic methods. As a result of this obstruction, wheezing or stridor ensues. At first emphysema is noted when the growth is small, but as complete obstruction develops atelectasis results, and the stage is set for severe bronchiectasis. It is then that the fever becomes more constant, or recurrent.

From the diagnostic point of view the best tool is the bronchoscope, through which most of these tumors can be visualized, and through which biopsy can be taken. In a series of 86 patients with bronchial adenomas at the Mayo Clinic reported by Moersch and McDonald,[14] 84 were bronchoscoped, and 78 gave positive biopsies.

TABLE I — SUMMARY OF 21 CASES OF BRONCHIAL ADENOMAS IN CHILDREN

CASE NO.	SEX	SYMPTOMS BEFORE DIAGNOSIS	AGE (YRS.) AT DIAGNOSIS	SITE	NATURE OF TUMOR	TREATMENT	FOLLOW-UP	COMMENT	REF. NO.
1	M	—	4	Left lower	"Adenoma" involving hilar lymph nodes	Endoscopy, Pneumonectomy (for recurrence)	Well 2 yrs.	Physical findings out of proportion to symptoms	2
2	M	7 mo.	6	Left main	"Polyp"	Endoscopy	Unknown	Post-pertussis wheezing and cough	9
3	F	2 yr.	6	—	"Polyp"	Pneumonectomy	Well some months	7 attacks of left basal pneumonia and atelectasis	16
4	M	6 mo.	7	Left main	Sessile "adenoma"	Endoscopy, Pneumonectomy	Well 3 mo.	Recurrent left lower lobe pneumonia and atelectasis	24
5	F	1 yr.	8	Right main	? Cylindroma	Endoscopy, Pneumonectomy for residual after 2 mo.	Well 2 yrs.	Migrating right sided pneumonia. First diagnosed carcinoma	1
6	F	1 yr.	9	Right lower	Polypoid carcinoid	Repeat Endoscopy, Pneumonectomy at 6 mo. (stenosis)	Well more than 2 years	Seropositive Negro: Middle lobe syndrome: First biopsy negative	18
7	M	2 mo.	9-9/12	Left lower	Infiltrating carcinoid	Endoscopy, Lobectomy		6 relapses of cough and fever. Persistent atelectasis	This report
8	M	9 mo.	11	Right main	"Polyp"	None: coughed up during endoscopy	Re-expansion after 2 mo.	Admitted suspect tuberculosis	17
9	M	—	11	—	"Adenoma"	—			15
10	F	—	11	Carina, left upper	Adenoma	Endoscopy, Bronchotomy	Well 4 yrs.		23
11	F	2 yr.	12	Right upper	? Carcinoid	Lobectomy, Radiation	Well 1½ yrs.	Clinical diagnosis: bronchostenosis	7
12	F	2 yr.	12	Left lower	Sessile Jackson-type	Endoscopy, Bronchotomy	None	Relapsing fevers	5
13	F	2 yr.	13	Carina, left upper	Sessile basal cell type	Endoscopy	None	Increasing stridor	4
14	M	3 yr.	13	Right main	Jackson type	Endoscopy, Coagulation	Well 3½ yrs.	Cough, pneumonias	9
15	M	1 yr.	13	Left main	Infiltrating carcinoid	Endoscopy, Pneumonectomy	None	Persistent atelectasis, stridor	20
16	F	10 mo.	13	—	? Carcinoid	Endoscopy	? well over 18 years	? case reported twice by this author	19
17	F	6 mo.	14	Left main	"Polyp"	Endoscopy, Bronchotomy, Coagulation	Well 1 yr.	Wheezing, hemoptysis	6
18	M	4 yr.	15	Right lower	Sessile, papillary basal cell type	Repeated Endoscopy	Died during bronchoscopy	Pertussis age 6, repeated negative biopsies	10
19	F	2½ yr.	15	Right lower	Jackson type	Lobectomy	Well 4½ yrs.	Cough, pneumonia, empyema	8
20	F	5 mo.	15	Right lower	Jackson type	Endoscopy, Coagulation, X-ray	Minimal symptoms for 15 yr.	Cough, relapsing chills and fevers	8
21	—	—	15	—	"Adenoma"	—			14

In Soutter's series of 56 from the Massachusetts General Hospital,[21] 46 were positively diagnosed at the first bronchoscopic examination. Because the tumors are usually located in the main or major bronchi (as they may originate from the epithelium of the mixed glands or their excretory ducts), they are easily visualized except in upper lobe bronchi. In the cases of the 21 children here tabulated (Table I), one-half were found at the carina or in the main-stem bronchi, and the other half in the second division bronchi. No particular predilection for one lung or one lobe was noted. No case of peripheral adenoma is reported in this group. All but two cases were diagnosed by endoscopic biopsy. In two additional cases more than one biopsy was required to establish the diagnosis. One bronchoscopy was terminated because of hemorrhage from the lesion.

Sessile, protruding or polypoid, tan-pink, usually smooth-surfaced intrabronchial lesions may on visualization suggest a granuloma, a fibroma, hamartoma or an adenoma. Although the adenoma is very vascular and therefore bleeds very easily (especially the carcinoid type), ulceration or necrosis, as so often noted in carcinoma, is not at all common even with complicating infection or trauma. The sessile or broad-based lesions often extend through the bronchial wall in a dumbbell formation, or an iceberg configuration, making endoscopic excision both dangerous and difficult, or totally impossible. There is usually no fixation of the bronchus, as in carcinoma, although chronic infection may produce fibrosis with adhesions.

Bronchography may be of help in locating the exact site of the lesion, and also is helpful in determining the presence and degree of bronchiectasis. The tumor may be outlined as a filling defect. Sputum washings are rarely positive, as in cases of carcinoma, since the epithelial surface of the adenoma is usually intact. No case was found in which the diagnosis was made by this method.

In the presence of an equivocal clinical and histologic picture, diagnostic considerations must include certain tumors of childhood, most often arising in bone or retroperitoneally, such as embryoma of the kidney, Ewing's tumor or lymphoma. Support for this concept may be found in a group of tumors reported as carcinoma of the lung in children.[22]

Treatment has included endoscopic removal or coagulation, bronchotomy, lobectomy or pneumonectomy, and radiation therapy by radium, radon or x-ray. These methods of treatment have been well-discussed in the other papers. If the lesion is not situated at the

carina, lobectomy or pneumonectomy in the hands of an experienced thoracic surgeon seems to offer the safest and surest method of cure. The dangers of endoscopic removal or treatment, since these tumors are so vascular, and since they usually extend beyond the lumen of the bronchus, have been emphasized.

Ultimate prognosis revolves about the uncertainties of biologic behavior as correlated with histologic features, length of clinical observation and manner of treatment. One case of recurrent pneumonia in childhood appeared to benefit temporarily from irradiation prior to establishment of the diagnosis. Only one of these children is known to have died (at 15 years of age) in direct relation to the disease (during the last of several bronchoscopic examinations). In a few instances among these collected cases local recurrence, complicating bronchostenosis, or progressive bronchiectasis prompted energetic therapy after initial treatment. None of the 14 cases in which the length of clinical observation is recorded was known to harbor residual tumor; eight were observed for periods of two to 15 years. The only case stated to have involvement of hilar lymph nodes appeared free of disease two years after pneumonectomy.

The variability of pathologic interpretations raises major difficulties in evaluation of the biology of these tumors. At least three cases reviewed here included the term carcinoma in the diagnosis, one being diagnosed carcinoma outright by one observer and bronchial adenoma by others. Three reports of malignant pulmonary tumors in pediatric patients may be cited. Two or more of the 12 cases collected by Suter[22] may represent bronchial adenomas; this is particularly true of the lesion reported by Kanof.[11] The case (briefly summarized below) reported by Wasch et al[25] may represent a type of low grade bronchial carcinoma sometimes grouped with bronchial adenoma (cylindromas, basal cell tumors, or papillary adenocarcinomas, of which three other instances probably are included in this review). A tumor, composed of low cuboidal cells in crude glandular formations, was found in the right stem bronchus of an 11-year-old boy who gave a history of lower respiratory symptoms for six months. During the seven-year period of observation, therapy included several courses of irradiation by x-ray and radium. Terminal symptoms of congestive failure were preceded by development of an acromegalic habitus. Deposits of tumor were found in lymph nodes of the pulmonary hilus, in the opposite lung, in the kidney, and in the dura mater at necropsy. An eosinophilic adenoma of the pituitary was described in addition. This latter coincidence has been noted in other cases of adenomatous lesions of bronchi.

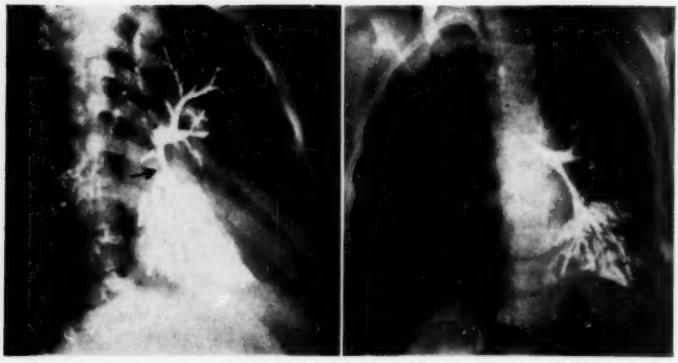

Fig. 1 A & B).—Radiopaque material demonstrates segmental clusters of dilated bronchi in medial portion of the left lower lobe. Local narrowing of the segmental bronchus is apparent. Post-biopsy study.

Classification (directed more to assessment of growth potential rather than to differentiation of histologic types of tumors) was attempted on these collected tumors according to the criteria of Liebow[13] as (a) carcinoid or Jackson-type adenomas and as (b) cylindroma or basal cell-like tumors. There were ten of the former and three of the latter. Three lesions were set apart as not fulfilling the explicit criteria of Liebow for either type. These have been considered as adenomatous polyps and are polypoid tumors of main stem-bronchi composed of glands or acini in scant avascular stroma, lined by pale, sometimes vacuolated or ciliated, tall cylindrical cells with basal nuclei surrounding masses of mucinous or calcific material. Five cases were described only by the unqualified diagnosis of adenoma. In one patient abnormal pulmonary architecture (possibly developmental) was noted in addition to the tumor.[16]

The range of ages in which these tumors produced symptoms or were diagnosed may be taken as further support for the hypothesis of hamartomatous or embryologically mediated development of these lesions.

REPORT OF A CASE

R.B., Jr. This 9 9/12 year old white boy was admitted to the Children's Medical Center of Boston on August 19, 1957, with a story

of six recurrent episodes of high spiking fever and cough over a period of eight weeks. After a few days of a mild upper respiratory infection, he developed a rapid rise in temperature to 104.6 on June 22, 1957. His temperature continued to spike daily for a week, although with a gradual general decline. A troublesome cough persisted. No specific treatment was given, as it was considered a virus infection. After three to four days of normal temperature and improvement in the cough, his fever recurred, suddenly rising to 104.4, with cough and development of malaise and general aches and pains. He was put on Tetracycline® suspension, one teaspoon four times a day for a few days. His temperature gradually declined to normal, where it remained for another four days, only to start spiking for a third episode four days later. There was also accentuation of the cough. After another four days he seemed to be normal, and the cough disappeared. On July 17 a fourth episode of spiking fever to 104 occurred with a return of the cough and malaise for another six to seven days. X-rays at a local hospital showed a "homogeneous, rather large shadow of consolidation in the left lower lobe, consistent with atypical pneumonia." W.B.C. was only 7800/cu mm, polymorphonuclears 66%, lymphocytes 27%, monocytes 6%, bands 1%. Hgb. 13.5 gm%. Heterophile agglutinations for mononucleosis were negative. Typhoid-dysentery agglutinations were also negative. It was felt that no further antibiotics were indicated. From July 27 until August 1 he had a fifth episode of fever, but the temperature rose only to 101. From then until admission he had a fever from 99.4 to 101 on occasions. X-rays five days prior to admission at a second hospital showed the same area of consolidation in the left lower lobe, and the question of aspiration of foreign body was raised. Atelectasis of the lobe was reported.

The only medication the patient had received was Tetracycline early in his course. At no time had he had chills, productive sputum, hemoptysis, wheezing or chest pain. There had been no known exposure to tuberculosis, although the paternal grandmother had died of tuberculosis 25 years beforehand.

On examination the boy was in the 50th percentile for height and 10th percentile for weight. He did not appear acutely ill. Temperature was 100° F, pulse rate 114/min., respiratory rate 25/min.

Except for his liver which was palpable one and one-half inches below the costal margin, the positive findings were limited entirely to the chest. Diminished breath sounds with dullness and decreased fremitus were found at the left thoracic base. Occasional rales and

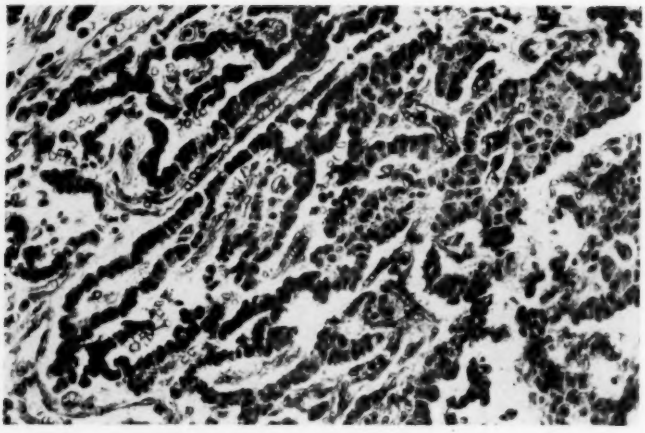

Fig. 2.—A typical area of the tumor found on biopsy. (Zenker's fixation. Toluidine blue-eosin. x 270.)

rhonchi were heard throughout the chest. Admission laboratory data were as follows: Blood: Hgb. 12 gm%; WBC: 12,400/cu mm; polymorphonuclears 85%; lymphocytes 10%; monocytes 1%; eosinophils 3%; metamyelocytes 1%; tuberculin (1:100): negative; gamma globulin: 1.1 gm%. Throat culture: negative. Nose culture: few staph. aureus. Urine: entirely negative. Roentgenograms showed inflammatory infiltration involving the left lower lobe, with considerable diminution in volume, suggesting inflammatory atelectasis. Whether this represented a chronic pneumonitis associated with obstruction from a non-opaque foreign body, or residual of a recent viral pneumonitis, could not be determined. No hilar glands were noted.

On August 21 bronchoscopy was carried out under ether anesthesia after premedication with nembutal and atropine. A No. 5 bronchoscope was used. Considerable foul pus was noted in the larynx and trachea, and about 30 ml of extremely thick brownish purulent material were aspirated from the left main and lower lobe bronchi. The material was so thick it kept plugging the suction tip, and would not run down the side of the collecting tube. The mucosa on the left side was red and granular. On the medial wall of the lower lobe bronchus about 5 cm from the carina, and about 1 cm below the upper lobe orifice was noted a reddish-purple granuloma-

Fig. 3.—Magnified view of the site of the lesion on the surgical specimen showing both intraluminal and mural aspects (longitudinal section).

tous mass which was friable and bled very easily and very profusely when touched with the suction tip. It nearly occluded the bronchial lumen. As much of the mass as possible was removed. No foreign body was seen below it, but bronchiectasis was considered to be almost certainly present. About 6 ml of lipiodol was injected into the left lower lobe bronchus. Bronchograms (Figs. 1A and 1B) showed all the segmental bronchi in the left lower lobe to be closely approximated, with moderate dilatation and bronchiectasis. The left lower lobe bronchus seemed narrow and irregular from either secretions or granulations. The roentgenologic diagnosis was "atelectasis and bronchiectasis of the left lower lobe, with stenosis of the left lower lobe bronchus." B. subtilis and H. influenzae grew in culture of bronchial aspirate. Pathologic diagnosis of the biopsy was "bronchial adenoma." For a few days penicillin aerosol therapy and postural drainage were carried out.

On August 28 Dr. Robert E. Gross performed a left lower lobectomy under endotracheal ether anesthesia. A sixth interspace incision was made. After splitting the interlobular fissure, no tumor was felt externally, and frozen section of a few enlarged glands showed chronic inflammation but no tumor. The bronchus was cut

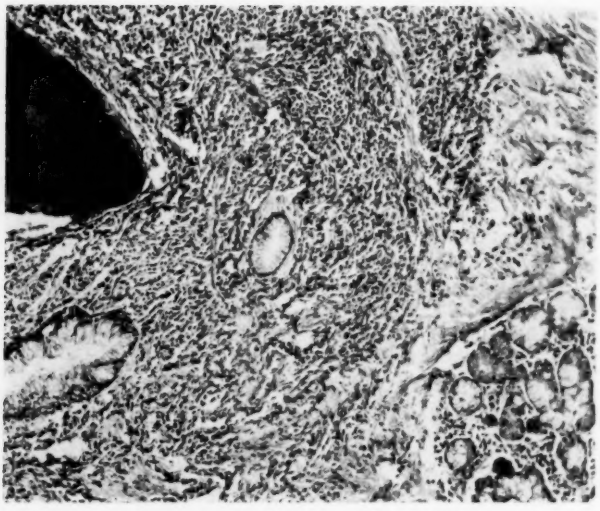

Fig. 4.—Midbronchial wall showing residual tumor (left) containing bone and duct-like structure and uninvolved bronchial glands (right). (Klotz fixation. Hematoxylin-eosin. x 135.)

just a few millimeters above the tumor. The pathologic diagnosis on the specimen was: "bronchial adenoma, chronic pneumonitis, and obliterative bronchitis." His postoperative course was entirely satisfactory, and the patient was discharged on the ninth postoperative day. Follow-up examination six months after surgery showed that he had been entirely asymptomatic since discharge.

Pathologic Findings. The soft, pinkish-gray hemispherical biopsy (8 by 5 by 3 mm) had a smooth, glistening, convex surface. Microscopically, a chronic inflammatory reaction lay in submucosa beneath essentially intact or metaplastic bronchial mucosa and merged with masses of tumor which extended to the margins of excision. The tumor (Fig. 2) consisted of small, regular cuboidal or low columnar, non-ciliated epithelial-type cells. These were arranged in irregular long chains along delicate fibrovascular septa in single rows or less commonly in double rows outlining indistinct or potential tissue spaces. The spaces sometimes contained wisps of pale secretory matter staining gray-blue with toluidine blue eosin. Occasionally more solid cellular patterns were found suggesting a monocellular plate cut parallel to the surface plane. The cytoplasm was diffusely and

minutely stippled with gray-purple after Schmorl's stain but was considered negative for true argentophilia, was red with aniline blue-orange G, and was dark blue-purple with phosophotungstic acid hematoxylin. The nuclei were small, regular, usually centrally placed, and dark without evidence of mitosis. Heavy clumps of chromatin lay in relation to nuclear membranes and single nucleoli were common. Irregular masses of cartilage and bone were present in the deeper portions of the biopsy. Structures resembling ducts of bronchial glands appeared caught in the superficial portions of the tumor.

The proximal segment of the dilated stem bronchus obtained with extirpation of the left lower lobe of the lung was filled with fibrino-purulent exudate attached to an area of mucosal roughening and protrusion (Fig. 3). Beneath this area the bronchial wall had the appearance of fibrous thickening with an irregular zone of crisp pink and yellow tissue (5 by 2 by 3 mm) extending just through the wall well away from the margin of excision. Microscopically bronchial mucosa had largely healed the biopsy site. Tissue similar to that of the biopsy (Fig. 4) (also containing metaplastic bone and structures resembling ducts of bronchial glands) lay predominantly in the middle third of the bronchial wall and locally infiltrated along bronchial adventitia. Lymphatic and vascular invasion was not recognized apart from the local adventitial involvement, and sections of enlarged hilar lymph nodes contained no tumor.

SUMMARY

The first case of bronchial adenoma recognized at the Children's Medical Center in Boston is described. Twenty cases diagnosed in the age group up to 16 years are collected from the literature.

These lesions are believed to include bronchial adenomas of the carcinoid, cylindroma and adenomatous polyp types. There is no clear evidence that the biology of the disease differs materially among adults or children. A trend to earlier diagnosis of these lesions may parallel increasing medical awareness of the problem, will decrease a certain porportion of chronic pulmonary invalidism, and may require revision of concepts of age of onset. The youth of these patients at the time of diagnosis supports the concept that some of these lesions may be related to local developmental abnormalities.

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LXXXV

THE ART AND SCIENCE OF BRONCHOGRAPHY IN INFANTS AND CHILDREN

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(By invitation)

AND

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The effective treatment of many conditions of the cardiorespiratory and upper gastro-intestinal systems in the pediatric age group first requires a precise diagnosis. This must include a consideration of the anatomic and pathophysiologic features as well as the etiology of the disorder. Certain diagnostic modalities provide information of this type; bronchography in children is one which has proved useful in our experience. The contrast roentgenogram also serves as a permanent visual record of the disease process.

A total of 92 bronchograms made during the past five year period at Children's Hospital of the East Bay and Highland-Alameda County Hospital have been reviewed. Comments and experiences of the members of the radiology, pediatric, anesthesiology and thoracic surgery staffs have been incorporated. Since bronchography is a technical procedure and the performance of such studies in children presents problems unique to these little patients, some methods have yielded more satisfactory results than have others. A discussion of these techniques, the art and science as it were, is the purpose of this report.

METHOD

In children, bronchography is performed under light general endotracheal ether anesthesia supplemented with a topical agent such as cocaine or Xylocaine.® Bronchoscopy usually precedes intuba-

From the Thoracic Surgery Services of Children's Hospital of the East Bay and Highland-Alameda County Hospital, Oakland, California.

tion. Induction of anesthesia and bronchoscopy are done in the operating suite; the patient is then transferred to the radiology department accommpanied by the anesthesiologist and surgeon where under the direction of the radiologist, the bronchogram is performed.

The agent used is Dionosil Oily® and limited volumes (5-10 cc) are injected through a small plastic catheter passed through the lumen of the indwelling endotracheal tube. Laryngospasm and anoxia are prevented in this manner. Unilateral studies under fluoroscopic control are made, following which as much of the contrast media as possible is removed by suction through the catheter. When indicated, contralateral studies are then made in the same fashion. Postero-anterior and oblique films are made of each side. A lateral view of the first side is taken. With fluoroscopy, an image intensifier is desirable. Following removal of the media, the child is allowed to recover from the anesthetic and the endotracheal tube is removed. During the following twenty-four hour period, an intermittently cool moistened atmosphere is provided.

GENERAL CONSIDERATIONS

A bronchographic study in this manner requires the co-operative efforts and skills of all concerned. Each participant must work with celerity and competence within his own scope, and must be aware of the patient's cardiorespiratory status in the darkened room. A stethoscope which may be moved to prevent obstructing the radiographic field is taped to the chest, and observations of breathing and cardiac activity are made each time the fluoroscope is used. It is possible to increase the light in the room to some extent if an image intensifier is used. The selection of a proper endotracheal tube for the age and size of the child is important. The tip of this tube should lie well above the carina, not in one of the main bronchi. Anesthesia is light enough so that continued spontaneous respirations are always present. The cough reflex is so subtended that deeper general narcosis is unnecessary. Secretions are removed as they form, and endotracheal suction is gentle and intermittent to avoid reduction of the tidal air volume. The signs of anoxia may be difficult to discern under the circumstances and these simple but important precautions to prevent such a state should be observed.[1,2]

Radiation exposure is kept at a minimum and the image intensifier is valuable in this regard. Since respirations are not stopped, an extremely fast exposure time is necessary; 1/60th of a second is used

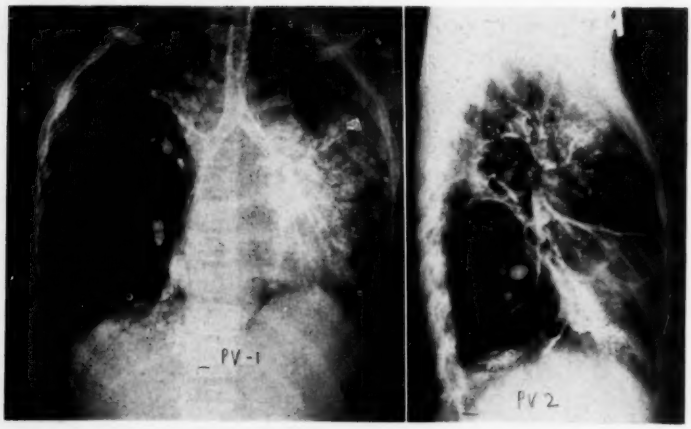

Figure 1

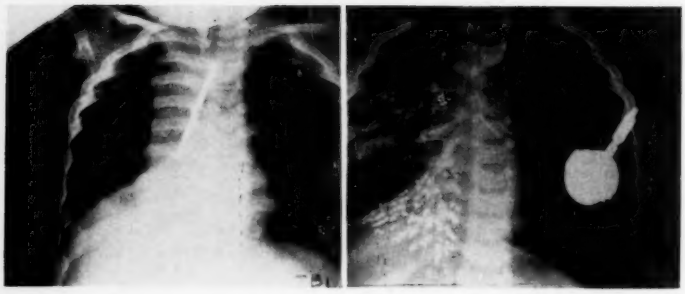

Figure 2

for spot films as well as the conventional views. The radiologist is familiar with the fluoroscopic patterns of the bronchial tree and is prepared to take spot films of suspected abnormal areas. He determines the extent of bronchial coating both in degree and distribution and directs the necessary positioning.[3]

The surgeon injecting the radiopaque agent is sufficiently familiar with the fluoroscopic patterns to work in accord with the radiologist. Injection of the media corresponds to the inspiratory

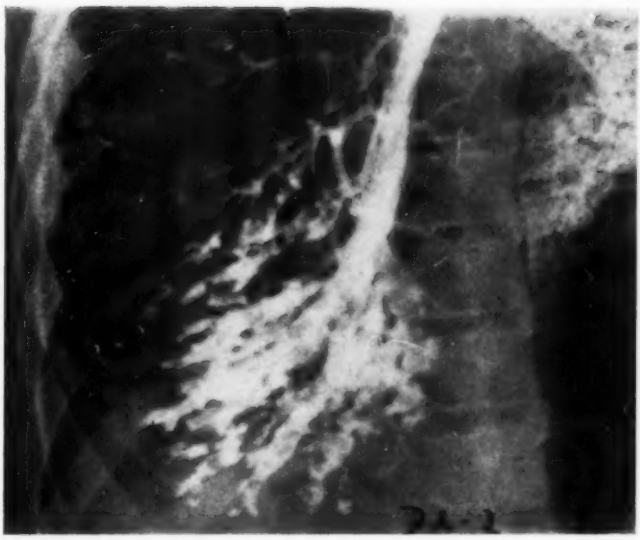

Figure 3

phase of respiration. The prime consideration should be to keep the volume of injected material at an absolute minimum for an adequate study and to remove as much as possible by suction under the fluoroscope upon completion of each side particularly in the smaller child. In infants, it is entirely feasible to produce a satisfactory bronchogram with 5 cc or less. Bronchial coating, which gives a double contrast roentgenogram and causes less ventilatory impairment is more to be desired than is bronchial filling.

The concept of physiological bronchography[4] which is utilized in adults under local anesthesia can be applied only to a limited extent under general anesthesia. When physiologic techniques are used, one depends upon the deliberate inhalation of contrast media from the major bronchus into the peripheral bronchi as well as upon gravity and positioning. Under general anesthesia, one does not have the co-operation of the patient this technique requires. Peripheral segmental filling is consequently more haphazard and less reliable diagnostically. With Dionosil Oily, however, respiration even under general narcosis, causes a peripheral flowing of the contrast media which is seen fluoroscopically. This allows segmental delineation,

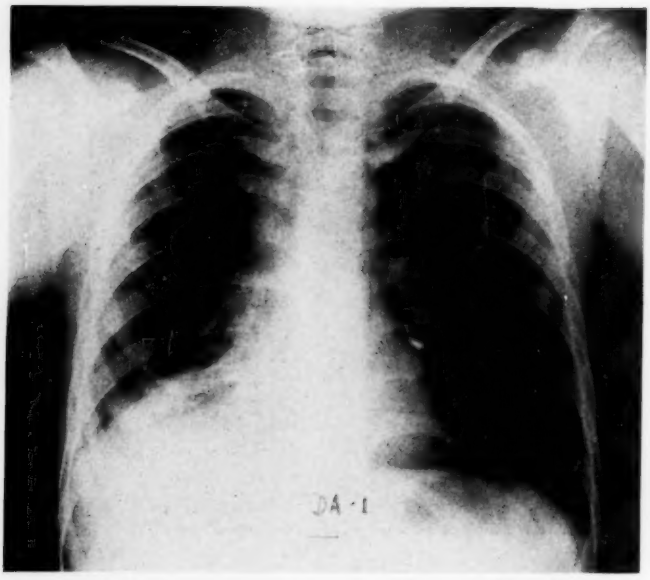

Figure 4

possibly at the expense of extreme contrast seen with some other agents. Actual volumetric filling of the bronchial tree with Dionosil may give greater contrast, but in children is physiologically undesirable. Although the quality of reduced viscosity of Dionosil which accounts for its coating and flowing characteristics is an advantage, it presents one serious technical problem. Should the anesthesia bag be compressed after instillation of the agent, the material may be blown out into the alveoli, and radiographic obscuration of the lung field result. The same may occur to a lesser extent with coughing (Fig. 10). Relatively light general anesthesia with an additional topical agent makes it unnecessary to assist respiration and prevents cough.

INDICATIONS

The history, physical examination, laboratory and routine roentgenographic studies are sufficient in many instances for the evaluation of pulmonary disorders; in others, they will present the physician with additional unanswered questions which may be solved by endos-

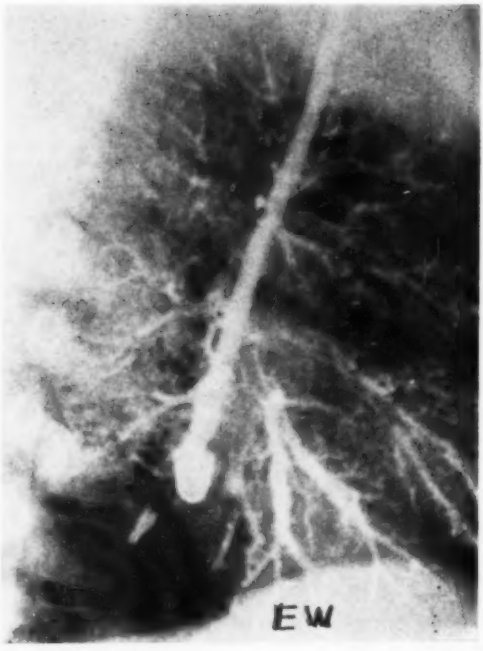

Figure 5

copy, bronchography, or both. Ferguson and Flake have discussed the clinical symptoms which require more than routine evaluation. They list roentgenographic evidence of chronic pulmonary changes, chronic cough which is unexplained, stridor, recurring infection (particularly in the same pulmonary area), localized wheezing and hemoptysis.[5,6]

The basic pathology is often best defined by the bronchogram when certain roentgenographic findings are present. Among these abnormalities, atelectasis, persistent pneumonitis, obstructive emphysema (air trapping with or without mediastinal shift) and hemithoracic contraction are especially important.

Tracheal or bronchial obstruction due to a vascular ring, congenital anomaly, focal cartilaginous infection or maldevelopment, inflammatory stricture, eroding nodes or middle lobe syndrome may be the cause of stridor, wheeze, or recurrent pulmonary infection. Such

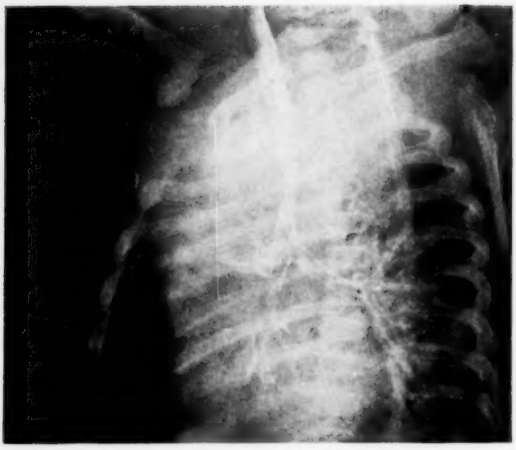

Figure 6

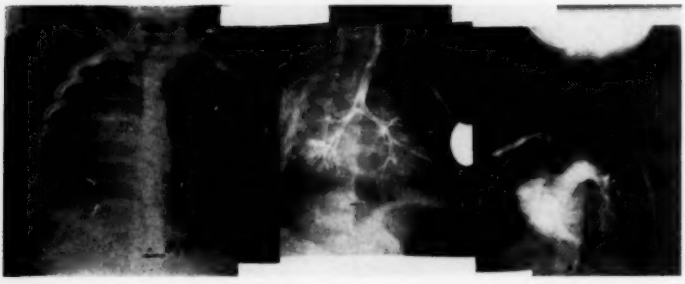

Figure 7

disorders may be shown bronchographically.[7,8] Tuberculosis causes one or more of these lesions[9-12] and bronchography is valuable in the study of the disease in children.[13,14] Extrinsic bronchial encroachment or widening of the carinae depicted by the contrast effect of the bronchogram may strongly suggest the presence of mediastinal lymphadenopathy, tuberculous or nonspecific.[15] In the category of obstructive lesions the combined observations made by endoscopy and by contrast radiography are particularly significant.

Congenital abnormalities involving both the trachea and the esophagus, tracheo-esophageal fistulae and strictures, may also be demonstrated.[16]

Suspected bronchiectasis is the time-honored indication for bronchography. In this study, the highest incidence of normal bronchograms was found in the group of patients with unexplained cough and suspected bronchiectasis. Such an investigation is justified, however. The finding of an architecturally normal bronchial tree in the absence of laryngeal abnormality may make a diagnosis of allergy or habit cough more tenable.

Our experience would indicate that a bronchogram should be performed to complete the evaluation of the lungs when foreign bodies have been aspirated, particularly when they have been retained for any appreciable length of time (Fig. 2). These examinations should be bilateral. Severe bronchiectasis has been found on one side in cases in which the foreign body had recently migrated and had been removed from the opposite lung (Fig. 3). Occasionally, foreign bodies which are inaccessible on bronchoscopy may be localized by bronchography (Fig. 5).

REPORT OF CASES

The following cases have been selected to illustrate bronchographic findings in various disease processes.

CASE 1. (Fig. 1) P.V., an eleven year old Philippine girl, had been chronically ill most of her life with a cystic condition of the right lung which had been discovered at one year of age. Her clinical status was that of chronic suppuration and hypoxia and she weighed only 51 pounds.

On routine x-ray examination, there appeared to be at least two large cysts with fluid levels. Bronchoscopy revealed no evidence of bronchial stenosis and the secretions appeared to be coming from the right lower lobe.

The bronchogram is shown. The large cystic areas on the right are seen with cephalad compression of the upper lobe, displacement of the middle lobe, and encroachment upon some of the basilar segments of the lower lobe. Dionosil readily entered the cyst suggesting patent bronchial communications. The left lung appeared uninvolved.

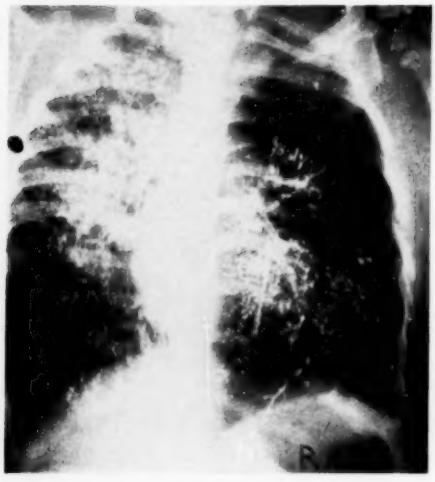

Figure 8

At surgery the cyst was composed of almost the entire lower lobe which in its overdistended state had pushed the upper lobe well into the apex and had separated upper and middle lobes along the horizontal fissure so that the middle lobe was lying anteriorly and inferiorly. A right lower lobectomy was performed.

In this instance, the bronchogram aided in localization of the cystic areas and demonstrated the uninvolved but compressed areas of lung on the right and normal lung on the left. It is now one year since surgery and the patient has made an excellent recovery.

CASE 2. (Fig. 2) J.B. The bronchogram demonstrates bronchiectasis and atelectasis of the right lower and middle lobes. This was caused by the presence of a foreign body, a metal nail, in the bronchus for one year. Following the removal of the foreign body bronchoscopically and determination of the pathological status of the lung bronchographically, a right lower and middle lobectomy were done.

CASE 3. (Figs. 3 and 4) D.A., a nine year old boy, had had atelectasis of the right lower lobe with pneumonitis for a period of one and a half months. Bronchoscopy revealed secretions coming from an inflamed right lower lobe. No foreign body was seen on

bilateral examination. The bronchogram demonstrates extensive bronchiectasis of the right middle and lower lobes (Fig. 3).

After clearing of the bronchographic agent a postero-anterior roentgenogram revealed retention of radiopaque media localized in the left lower lobe bronchus as well as the previous findings (Fig. 4).

At the second bronchoscopy a foreign body consisting of a tooth-paste tube cap filled with Dionosil was removed from the left side where it had apparently migrated. The right middle and lower lobes were subsequently removed and an uneventful recovery made. Bronchography of the left side showed no residual bronchiectasis.

CASE 4. (Fig. 5) E.W. Lateral bronchogram demonstrating a foreign body (pencil cap) obstructing a basilar segmental bronchus of the right lower lobe. The foreign body was inaccessible bronchoscopically and was removed by pneumonotomy.

CASE 5. (Fig. 6) C.V. Tracheobronchogram demonstrating a defect in the lower third of the treachea in a patient with stridor. A vascular ring with an anomalous left innominate artery crossing the trachea anteriorly at this point and a constricting ligamentum arteriosus were found. The anomaly was repaired with complete relief of symptoms.

CASE 6. (Fig. 7) A.L., a three year old girl, who had had repeated pulmonary infections on the right, was found to have marked congenital hypoplasia of the right main pulmonary artery with systemic arterialization of the right lung. Pre-operative studies, including bronchography, excluded the possibilities of agenesis or atelectasis on the right or obstructive emphysema on the left. Angiocardiography showed no demonstrable filling of the right main pulmonary artery. Right pneumonectomy was performed. The patient unfortunately succumbed to an intractable hemorrhagic diathesis.

CASE 7. (Fig. 8) R.A., an 18 month old infant, developed dyspnoea at three months of age. A left thoracotomy performed elsewhere revealed no abnormality. It was thought following this operation that there might be agenesis of the right lung and a bronchogram was suggested. The patient's symptoms improved, however, until she learned to walk when dyspnoea with exertion recurred. Marked overexpansion of the left lung with compression of the right lung was found on x-ray examination.

Figure 9

Bronchoscopy demonstrated a definite collapse of the left main stem bronchus at and above the upper lobe orifice. No intrinsic stenosis was present as a No. 3 bronchoscope could be passed through this area.

Bronchogram demonstrates the presence of an essentially normal but compressed right lung. The collapse of the left main bronchus and marked emphysema of the left lung is shown. Delayed clearing of the contrast media in subsequent films was demonstrated.

Left thoracotomy was performed and a large bullous lung with cystic degeneration of the lower lobe and a very small left pulmonary artery were encountered. A left pneumonectomy was done. Microscopic sections revealed distention of the alveoli with thinning and frequent rupture of the interalveolar septa. The patient has done well postoperatively.

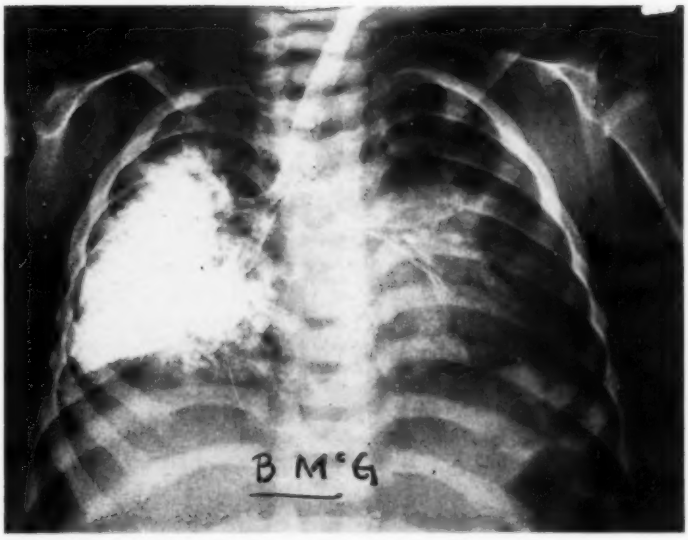

Figure 10

CASE 8. (Fig. 9) S.P., a three year old boy, presented with a pulmonary infection of one month's duration characterized by persistent pneumonitis at the left base and low grade fever. Although the left lung field was resonant to percussion, breath sounds were absent on this side. On bronchoscopy an eroding tuberculous lymph node almost completely obstructing the left main bronchus below the carina and above the upper lobe orifice was encountered and removed. The bronchogram demonstrates extrinsic compression of the left main bronchus with widening of the carina and the sinus remaining following evacuation of the node. There are irregularities of some of the basilar bronchi in areas of pneumonitis suggesting segmental obstruction and an area of extrinsic compression of the left lower lobe bronchus presumably due to tuberculous nodes.

CASE 9. (Fig. 10) This bronchogram demonstrates one of the more serious technical problems of bronchography under general endotracheal anesthesia. Following instillation of the contrast agent, the anesthesia bag was compressed manually to supplement respiration. The media was dispersed out into the alveoli by the augmented air flow and radiographic obscuration of the lung field was the result.

Practically none of the Dionosil could be recovered by suction and mild dyspnoea persisted for two days followed by recovery and clearing of the roentgenogram. This problem may be avoided by the use of proper anesthesia technique.

COMMENT

Co-operative teamwork in the performance of bronchography under general anesthesia has been stressed. The advantages of this method in children are obvious: Facility and controlled maintenance of an adequate airway are perhaps the most significant. Psychological trauma is minimized. The relatively small diameters of the trachea and bronchi as well as the effects of certain disease processes in individual patients seriously reduce the margin of safety allowable with ventilatory impairment.

When the technical considerations are carefully appraised, it is evident that the provision and maintenance of an adequate unobstructed airway is desirable in order to produce a satisfactory bronchogram as well as to assure the safety of the patient.

In the sequence of investigative procedures applied in the evaluation of pulmonary disorders, bronchography is seldom the initial study indicated; it is frequently, however, the final one required. Often the bronchogram offers a definitive diagnosis; it frequently adds confirmatory information; when technically well done and pathologically negative, it contributes by the process of exclusion. As with other types of radiographic examination, the interpretation of a technically unsatisfactory film is not justified. The relative complexity of bronchography as a radiographic procedure makes it difficult to repeat for the sake of quality, and every effort should be made to achieve an initial satisfactory study.

SUMMARY

A precise diagnosis of conditions affecting the bronchopulmonary, cardiovascular and upper gastro-intestinal systems in infants and children has become increasingly important since successful methods of treatment have developed. Bronchograms are valuable and often indispensable in making such a diagnosis.

The authors review their experience over a five year period. In the pediatric age group, specialized techniques are necessary to pro-

duce satisfactory bronchograms. A method which offers a high degree of safety to the patient and permits bronchography of good diagnostic quality has been used and is presented in detail. Illustrative studies of various pathological conditions are presented.

459 30TH ST.

ACKNOWLEDGEMENT—The authors wish to thank Dr. David J. Dugan and Dr. J. Hallam Cope for permission to describe cases D.A. and R.A., and case J.B.; also members of the Departments of Anesthesia and Radiology.

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LXXXVI

PERFORATION OF THE ESOPHAGUS

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According to our studies and those of others, traumatic perforation of the esophagus is on the increase;[2,4,19,20] due primarily to the increased frequency of esophageal instrumentation in the diagnosis and treatment of lesions of the esophagus and stomach. Seybold et al,[19] in a study of 50 cases at the Mayo Clinic, reports 21 in the 36 years prior to 1942 and 29 cases in the 7 years through 1949—a sevenfold increase.

Because of this increased incidence, thoracic and general surgeons alike are called upon more frequently to confirm the diagnosis and institute proper therapy. Although the potential dangers of this catastrophe are well known, there is little agreement regarding proper therapy; some advocating immediate surgery and others employing a more conservative approach.[1,13,14] In an attempt to shed more light on this problem, we have recently studied a group of cases treated in the San Francisco Bay area.

Our material consists of 54 cases. There were 21 perforations in the cervical region, 16 in the upper thoracic region and 17 in the lower thoracic (Table I). There were 11 deaths, a mortality of 20 per cent, with the highest mortality in the lower thoracic perforations. The ages by decades are shown in Table II, with the largest number of cases in the first decade, though all ages are represented. Table III illustrates the etiology. Of the 54 cases encountered, 18 were due to esophagoscopy, 6 were secondary to dilatation, 4 due to biopsy, 1 due to gastroscopy and 1 after lavage, for a total of 30. That is to say, over half of the cases were due to esophageal instrumentation; the remaining 24 being due mainly to foreign bodies, though there were 5 cases of so called "spontaneous" or postemetic rupture and 4 cases

TABLE I

LEVEL OF PERFORATION

LEVEL	NO. OF CASES	DIED	PER CENT
Cervical	21	2	10%
Upper Thoracic	16	4	25%
Lower Thoracic	17	5	29%
TOTAL:	54	11	20%

TABLE II

AGES BY DECADES

AGE	NO. OF CASES	DIED	PER CENT
0-10	13	4	31%
11-20	3	0	—
21-30	2	1	50%
31-40	6	2	33%
41-50	6	0	—
51-60	10	1	10%
61-70	7	0	—
71-80	5	3	60%
81-90	2	0	—
TOTAL:	54	11	20%

due to violence either external or internal; such as the patient who attempted self bouginage with a straightened wire coat hanger.

The diagnosis is dependent upon a number of factors, the most important of which is a high index of suspicion. Pain, subcutaneous emphysema of the neck, fever and dysphagia with respiratory and circulatory embarrassment were encountered in most of the cases. The radiologic findings are those of mediastinal emphysema with or without pleural involvement. A swallow of a radiopaque medium is a useful method of localizing the level of perforation.[7,11] Naso-

TABLE III

ETIOLOGY

CAUSE	NO. OF CASES	DIED	PER CENT
Esophagoscopy	18	2	11%
Dilatation	6	3	50%
Foreign Body	15	2	13%
Gastroscopy	1	0	—
Spontaneous Rupture	5	2	40%
External Trauma	2	0	—
Internal Trauma	2	1	50%
Biopsy	4	1	25%
Lavage	1	0	—
TOTAL:	54	11	20%

gastric tubes should be passed under fluoroscopic control in order to insure proper placement.

Table IV represents the therapy employed in the cases studied in relation to the level of injury. None of the patients who had cervical lesions treated conservatively died, while one-third of those with upper thoracic lesions so treated expired and 40 per cent of the lower thoracic lesions died. Another interesting feature is that none of the patients treated by immediate open thoracotomy and repair died. It is apparent that lesions involving the pleura do poorly on conservative therapy, while some of those that involve the mediastinum alone may recover without surgical intervention. All of the patients received large doses of antibiotics. Multiple procedures were necessary in ten cases with one fatality. Two patients had a tracheotomy, four a feeding gastrostomy and one a jejunostomy.

It should be emphasized again that early recognition is the single most important factor. Since most cases occur after instrumentation, all of these patients should be watched with suspicion, particularly children, who may not complain of early symptoms. In one of our children under one year of age, the endoscopist realized that he had perforated the thoracic esophagus, turned the patient and accomplished primary repair immediately. In another infant the perfora-

TABLE IV

THERAPY EMPLOYED BY REGIONS

TREATMENT	REGION							
	CERVICAL		UPPER THORACIC		LOWER THORACIC		TOTAL	
	NO.PTS.	DEATHS	NO.PTS.	DEATHS	NO.PTS.	DEATHS	NO.PTS.	DEATHS
Conservative management	11	0	9	3	5	2	25	5
Cervical mediastinotomy	6	2	2	0	..	..	8	2
Posterior mediastinotomy	1	0	1	0	..	..	2	0
Closed drainage of pleural space	1	1	4	1	5	2	10	4
Open drainage of pleural space	1	0	3	0	4	2	8	2
Open thoracotomy with repair of esophagus	2	0	1	0	3	0	6	0
Primary resection	..	..	..	..	1	0	1	0

tion was discovered by x-ray showing a tube in the left pleural cavity immediately post esophagoscopy and an immediate repair was accomplished. Both of these children recovered uneventfully. There were two other children under one year of age in our series. Both of these had perforations of the thoracic esophagus following dilatation. These were unsuspected until high fever and signs of pneumothorax led to the diagnosis. Closed drainage of the chest resulted in death in both cases. Early recognition and repair would probably have saved these infants. Five of the 11 deaths in the series might have been prevented if a more aggressive approach had been adopted. On the other hand, those cases with demonstrated perforations of the cervical region in which the perforation was small and the lesion recognized early did well on conservative management, consisting of nothing by mouth, nasogastric suction, bed-rest and large doses of broad spectrum antibiotics.

Large tears of the esophageal wall, particularly those that involve the pleural cavity, are best treated by early open operation with repair and adequate drainage. Complete re-expansion of the lung is important in preventing empyema. A less radical approach may result in recovery, but the convalescence is long and complicated

by multiple drainage procedures. Although two of the five postemetic ruptures eventually recovered on conservative management, it should be noted that the pleural space had not been contaminated. There is no question that open operation is the procedure of choice here.

SUMMARY

Fifty-four cases have been studied.
The most frequent location was the cervical esophagus.
Instrumentation was the most frequent cause of perforation.
There were a total of 11 deaths in the 54 cases studied.

CONCLUSIONS

1. Early recognition is the single most important factor in the treatment of these lesions.

2. The therapy and prognosis depend on the location, size and duration of the wound, as well as the structures involved.

3. Conservative management of minor lacerations may be successful if therapy is undertaken before gross contamination and infection have taken place.

4. Larger perforations, especially those involving the pleural space, are best treated by early open operation with closure of the defect and establishment of adequate drainage.

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LXXXVII

RECENT ADVANCES IN THE DIAGNOSIS OF ESOPHAGEAL DISEASE WITH SPECIAL REFERENCE TO STUDIES OF ESOPHAGEAL MOTILITY

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The broncho-esophagologist has contributed greatly to our knowledge of the esophagus and its diseases. In recent years there have been improvements in the instruments available for esophagoscopy. Advances in anesthesia, developed in co-operation with our colleagues in anesthesiology, have made it possible for the esophagologist to perform a more satisfactory examination more safely than ever before. The procedure certainly is performed with less risk by competent specialists in the technique.

The broncho-esophagologist is able to recognize the various organic lesions of the esophagus and to describe them accurately. The pathologist has been of great help to the broncho-esophagologist in the study of organic lesions of the esophagus and upper portion of the stomach. By employing the quick frozen-section technique, the pathologist often is able to determine the nature of the lesion very shortly after the specimen has been taken for biopsy, perhaps even before the esophagoscope has been withdrawn.

The cytologic technique likewise has been of great help, especially in the recognition of carcinomas of the cardia which tend to encircle the lower part of the esophagus.[1] Although these lesions often cannot be seen at the time of esophagoscopy, smears from the region of the obstruction often will reveal malignant cells, while results of biopsy itself are negative. Special brushes have been devised to obtain material for cytologic study,[2] and material for smears also may be obtained from the flexible spiral that is used for bougienage.

USES AND LIMITATIONS OF ESOPHAGOSCOPY

Surely, esophagoscopy is the most important procedure in the recognition of strictures of the esophagus, malignant and benign

neoplasms and the various forms of esophagitis. The procedure also is extremely helpful in the diagnosis of esophageal hiatal hernia and esophageal varices. However, the various disturbances of function are less amenable to endoscopic diagnosis. Similarly, esophagoscopy makes a very limited contribution to the recognition of achalasia, diffuse spasm and incompetence of the esophageal sphincter. Direct examination of the esophagus likewise is of little value in the presence of functional dysphagia, globus hystericus, rumination and the like.

Actually, the broncho-esophagologist may learn more about these functional disturbances of the esophagus by passing a bougie over a thread which the patient previously has swallowed. Although bougies were designed primarily for therapy, they may provide valuable diagnostic information, especially if the blunt, olive-shaped bougie is used. When such bougies are passed into the stomach, a diagnosis of achalasia or diffuse esophageal spasm may be suggested by the nature and location of the resistance encountered. The sensation is very different from that noted when organic obstruction is present. This technique is of particular value when the patient is awake and sitting in a specially constructed chair.

PHOTOGRAPHY

Photographs of the esophagus through the esophagoscope have been made by some endoscopists for a number of years. Colored still pictures are excellent for the demonstration of organic lesions. However, cinephotography is of much greater value to our understanding of functional disturbances of the esophagus, especially if the films are run in slow motion. Recently, in France, improvements in light transmission by the use of the quartz-rod principle have made endoscopic photography both easy and practical.[3] It is hoped that much can be learned concerning functional as well as organic lesions of the esophagus.

ROENTGENOLOGIC AIDS

The roentgenologic examination always has been of great value in the diagnosis of esophageal lesions. This diagnostic aid is particularly useful when esophageal obstruction is present. The roentgenologic examination is helpful, again, in the diagnosis of esophageal hiatal hernias. However, the barium meal requisite to this procedure passes through the esophagus with great speed, and consequently it is very difficult for the roentgenologist to learn much about disturbance in function. Nevertheless, certain radiologists[4,5] have taken a particular interest in the esophagus, and have made real contributions to our knowledge of the physiology of the normal esophagus as well

as the various functional disorders of that structure. Because of the great speed of the esophageal component of deglutition, cineradiography would be an ideal method for the study of esophageal function, especially if the motion pictures could be shown in slow motion. Although cineradiography has been used for the study of the normal and abnormal esophagus, the usefulness of the procedure is limited by the hazards imposed by exposure to prolonged irradiation. The recent introduction of image-amplifier equipment should permit cineradiographic study of the esophagus without the risks of excessive exposure to irradiation. The value of presently available image-amplifier equipment is limited by the cost and bulkiness of the apparatus and the very small field that is available for visualization as well as for photography. Nevertheless, film strips of cinefluorography provide an excellent record of roentgenologic findings, and undoubtedly will prove very valuable as teaching aids.

PHYSIOLOGIC CONTRIBUTIONS

In recent years the greatest contribution to our knowledge of the normal esophagus and functional disorders of the esophagus has been made by the physiologist. Measurements of pressure within the esophagus and at the upper and lower sphincters of that structure have provided much information concerning the physiology of the normal esophagus, and such studies are helping us to understand the nature of a variety of esophageal disorders. Actually, the measurement of intra-esophageal pressure was begun in 1883 by Kronecker and Meltzer,[6] who recorded intra-esophageal pressure by means of balloons placed in the esophagus. Similar techniques were used in subsequent years by investigators such as Carlson[7] and Cannon,[8] and later by Ingelfinger and his associates.[9] The value of the balloon technique is limited by the fact that the balloon itself acts as a bolus. Thus, it was necessary to develop techniques of measuring pressure which do not stimulate the esophagus to contract.

For several years studies of esophageal motility have been carried out at the Mayo Clinic in the laboratory of physiology under the direction of Dr. C. F. Code. Measurements of esophageal pressure have been made with the aid of a tiny electromagnetic transducer identical to that used for the measurement of intracardiac pressures. The transducer can be introduced into the esophagus itself or the pressure changes can be transmitted to the transducer by means of a small, water-filled polyethylene tube which is passed into the esophagus. We have found it desirable to measure esophageal pressures at different levels within the esophagus simultaneously. For routine work we are now using three polyethylene tubes attached to three

electromagnetic transducers.[10] Measurements are made both at rest and after deglutition. Measurements of pressure are recorded on a photokymographic unit. The water-filled polyethylene tubes are joined together, but small notches are made at intervals of 3 to 5 cm, so that pressures can be recorded at different levels simultaneously. Records of esophageal motility have been made among a large number of normal persons, as well as persons with a variety of esophageal disorders. The findings have been reported in detail in a number of communications.

In the normal person these records of pressure give a clear picture of the function of the esophagus. As might be expected, the resting pressures within the esophagus are subatmospheric, but there is an increase in the resting pressure at both the upper and lower esophageal sphincters. The effort of swallowing initiates a peristaltic wave which requires about ten seconds to pass from the hypopharynx into the stomach.[11] The swallowing effort is followed by a relaxation of both the upper and lower sphincters.[12,13]

Our studies of achalasia would confirm the thesis that there is a neuromuscular disorder in this condition. In fact, achalasia is characterized by a motor failure of the esophagus associated with a failure of the lower sphincter of the esophagus to open.[11] Studies of motility show that the upper esophageal sphincter functions entirely normally. Resting pressures within the esophagus often are atmospheric. There is no evidence of a co-ordinated peristaltic wave. After deglutition there are only feeble increases in pressure and these are simultaneous throughout the esophagus. Of particular importance is the observation that there is no decrease in pressure at the lower esophageal sphincter after deglutition.[14] Thus the term, achalasia (failure to open), more nearly accurately describes the condition of the sphincter than does the term, cardiospasm. In fact, studies of resting pressures at the lower esophageal sphincter reveal that as a rule there is no more elevation of pressure in the sphincter in the presence of achalasia than there is when the esophagus is normal. Hence, as a rule there is no sign of spasm. After the subcutaneous injection of methacholine hydrochloride (mecholyl chloride), however, a striking elevation in pressure within the esophagus usually is demonstrated, often accompanied by substernal pain.[15] This phenomenon is not noted in normal persons or in patients who have other types of esophageal disorders.

OTHER CONSIDERATIONS

The clinical syndrome of diffuse spasm of the esophagus often is confused with cardiospasm or achalasia. This syndrome has been variously described as nonsphincteric spasm, segmental spasm, pseu-

dodiverticulosis, corkscrew esophagus and so on. Measurements of esophageal pressure in diffuse spasm[16] reveal that the resting pressures within the esophagus and at both the upper and lower sphincters are essentially normal, although the band of increased pressure at the lower sphincter is likely to be wider than normal, especially if an esophageal hiatal hernia is associated. After deglutition, the increases in pressure in the lower two thirds of the esophagus at various levels are simultaneous and much higher than normal. In other words, the orderly peristaltic sequence which takes place in the normal person is replaced by a spastic contraction of the lower two thirds of the esophagus.

Dysphagia is described as a symptom by at least ten per cent of all patients who have scleroderma. However, nearly all these patients are found to have a disturbance of esophageal motility when measurements of pressure are made.[17] When scleroderma is present, the upper esophageal sphincter functions normally. However, there generally is complete absence of peristaltic activity in the esophagus. The normal elevation in pressure at the lower sphincter is absent and there is no decrease in pressure at the gastroesophageal junction after an effort at swallowing. The findings certainly help to explain the frequency of regurgitation esophagitis in these patients.

Abnormalities of esophageal motility have been noted in a variety of other disturbances. Patients with Raynaud's disease have been studied, and their motility patterns are sometimes identical to those seen in scleroderma. As might be expected, there are disturbances of esophageal motility in patients who have suffered bulbar palsy and other neurologic disorders. Patients with esophageal hiatal hernia now are being studied, and it is probable that motility patterns will be worked out therefrom which will be of value in clinical diagnosis. Many patients are being encountered whose motility patterns do not fit into any well-recognized category. As the studies progress, it is likely that new entities will be described. Measurements of pressure are being used with increasing frequency in the evaluation of atypical thoracic pain, and it is hoped that as time goes on the method will prove increasingly helpful in differential diagnosis.

SUMMARY

In recent years the most significant contributions to our knowledge of the esophagus and its disturbances of function have been made by physiologists. Studies of esophageal motility have been carried out by the recording of pressures within the esophagus and at the sphincters of the esophagus. Patterns of esophageal motility have been

established for the normal person and also for patients who have achalasia, diffuse spasm and scleroderma.[18] The technique is being utilized in the evaluation of a variety of other esophageal disorders. These studies of esophageal motility have given us a better understanding of the normal physiology of the esophagus and have helped us to understand the nature of some esophageal disorders.

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LXXXVIII

LOCAL OR GENERAL ANESTHESIA FOR ESOPHAGOSCOPY, LARYNGOSCOPY AND BRONCHOSCOPY

AN EVALUATION OF 300 CASES

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It has been wisely said that medical remedies which are specific are well accepted. Those conditions with many and varied treatments are as yet unsatisfactorily resolved. To a large degree this is true for ear, nose and throat procedures requiring anesthesia for endoscopy and operative pharyngeal and laryngeal procedures. Here the interests of the surgeon, patient and anesthetist are often unhappily and sometimes disastrously met. Especially is this true in the adult who desires to be unconscious during the surgical procedure.

We wish to make clear at the onset that for a healthy, co-operative adult patient and a skilled endoscopist, local anesthesia is still the method of choice. In children, general anesthesia is preferable. For other situations, there is a great departure and lack of uniform method because of variations in surgical skills, capabilities of the anesthetist, patients' demands and complicating pathology. The subject of anesthesia for tonsillectomy in the child is a classic example ranging from chloroform with two minute guillotine amputations to endotracheal anesthesia and fascial dissection and minute blood vessel ligation. We wish further to emphasize that local problems and skills must always modify any recommended method for endoscopy and other airway procedures.

What are the most frequent requirements for endoscopy and pharyngeal-laryngeal surgery today?

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1. A wide open relaxed jaw.

2. A sleeping or heavily sedated patient, usually at his own insistence.

3. Adequate minute volume of respiration.

4. Simplicity.

When one recalls the time needed for some laryngeal and esophageal surgery or endoscopy, the anxious patient, the apneic situations produced by curare and barbiturates and cumbersome chest ventilators, the problem certainly requires a better solution.

We would like to present our experiences with an approach which utilizes the combined principles of local anesthesia, profound cerebral sedation, moderate analgesia and improved relaxation of the jaw without the serious depression of respiratory minute volume so common with intravenous anesthesia.

Such a method employs topical or local anesthesia and intravenous use of Hydroxydione and Demerol® (Meperidine). Hydroxydione (Viadril®) is a steroid similar to pregnandione and not too unlike cortisone chemically.

Selye first reported in 1941 on the central nervous system sedative properties of steroid compounds. Since then, over 10,000 administrations with Hydroxydione have been reported with widely conflicting claims. In brief, the pharmacodynamics of Hydroxydione is seen in Table I.

TABLE I

HYDROXYDIONE - PHARMACODYNAMICS

1.	Hydroxydione does not exert ordinary hormonal activity.
2.	In animals, nephrectomy or liver damage has not prolonged anesthesia or made it more profound.
3.	In animals, overwhelming doses to point of apnea does not abolish vigorous animal reaction to painful stimuli.
4.	ECG tracings in man indicate no change in rhythm.

TABLE II

HYDROXYDIONE

Diverse Opinons of Twelve Authors

RELAXATION OF JAW		ANALGESIA
EXCELLENT	5	BASAL SEDATIVE ONLY
FAIR	2	NO ANALGESIA (4)
PARTIAL	1	NO RESPONSE TO PAIN
NONE	1	PARTIAL ANALGESIA
NO OPINION	3	TRUE ANESTHETIC
		TRUE ANALGESIA

Table II will indicate some of the diverse opinions of 12 authors reporting on Hydroxydione. Diversity is not readily apparent from a perusal of one or two articles. This chart, for example, illustrates ideas expressed in the literature regarding one of Hydroxydione's supposedly singular properties, namely, relaxation of the jaw. One author stated that the jaw often needs to be pried open. The section to the right of the chart indicates feelings about analgesia. It is interesting that one author, who states it to be a true anesthetic, frequently complements its administration with cyclopropane. The majority believe that Hydroxydione is not unlike pentobarbital, i.e., hypnosis or presumed analgesia is related directly to the depth of sedation. Evidence is poor that it has true analgesic properties.

At our institution, Viadril was initially tried in a wide variety of surgical procedures with a diversity of complemental agents. It early became apparent to us that it has the following properties: 1) profound cerebral sedation, 2) usual pharyngeal and jaw relaxation comparable with deep ether anesthesia, 3) respiratory depression, though possible, often is present only to a minor degree when compared with other general anesthetic methods with comparable sleep and relaxation, 4) no influence on laryngeal function, 5) no analgesic properties, 6) hypotensive properties.

Where an appreciation of these properties has not been understood, variable rates of success have been reported. In addition, one must provide for pain relief and obtundation of vocal cord, laryngeal and tracheal reflex activity and maintain a continued awareness to respiratory and circulatory functions.

TABLE III

TYPES OF CASES

Bronchoscopy		10 Cases	
Esophagoscopy		19 Cases	
Adult Tonsillectomy		114 Cases	
Suspension Laryngoscopy		133 Cases	
			E.N.T. - 292 or 90%
Other Throat		11 Cases	
Palate	6		
Styloid	2		
Hypopharynx	3		
Facial Fractures & Burns		4 Cases	
Tympanoplasty		1 Case	
Perineal Surgery		33 Cases	- 10% non E.N.T.

Table III will indicate our preference for ear, nose and throat procedures when using Viadril.

Our techniques are as follows: premedication according to weight and age as for all general anesthetic procedures is employed. If the patient is to undergo a suspension laryngoscopy, bronchoscopy or esophagoscopy, the patient is placed in a chair and careful cocainization of the pharynx and larynx is performed. The patient is then placed in position on the ear, nose and throat table, an intravenous of 5 per cent glucose in water is begun with an 18 gauge needle in the largest accessible vein in the antecubital fossa. Veins of hand, wrist and feet are avoided because of a higher incidence of phlebothrombosis. With the intravenous solution running rapidly, 40 to 60 mgm of Demerol is injected which has been previously diluted 20 mgm/cc to which has also been added levallorphan in a 1 to 100 ratio. Levallorphan or Lorfan® is an antagonist to respiratory depression of narcotics which does not reverse the analgesic effects. This injection is followed with 40 cc of 2.5 per cent Hydroxydione solution or 1 gm. With 11 and 12 year olds, the Demerol is reduced to 20 to 40 mgm and Viadril 750 to 1 gm. In the large anxious or robust adult, 100 mgm Demerol has been used with up to 1500 to 1700 mgm of Viadril. For adult tonsillectomy and adenoidectomy procedures, the procedure differs as follows: on arrival in operating room, patient swallows a small quantity of one per cent Pontocaine

Jelly® rather than cocainization. After production of sleep and jaw relaxation, a Crowe-Davis mouth gag is introduced and from this point on, the tonsillectomy and adenoidectomy is done like a local procedure with peritonsillar local infiltration.

TABLE IV

VIADRIL - SUPPLEMENTAL DRUGS

Hydroxydione - Demerol - Lorfan	121 Patients
Hydroxydione - Demerol	105 Patients
Hydroxydione - Demerol - Nitrous Oxide - Curare - Wy-401 & Others	99 Patients

Table IV summarizes our various combinations tried. Onset of jaw relaxation occurs in about four minutes and full sleep and operative conditions are obtained in an average of seven to ten minutes. At this time it is possible to introduce the suspension laryngoscope, bronchoscope, esophagoscope or Crowe-Davis mouth gag with ease.

TABLE V

RESULTS

Completely satisfactory		274 Patients
Partially satisfactory		
Persistent cough	15	
Fair muscle relaxation	24	39 Patients
Failure		
No complimental analgesia	6	
Poor anesthetic technique	3	9 Patients
Required endotracheal tube for airway obstruction with onset of relaxation		3 Patients

As seen in Table V the state of relaxation and anesthesia is satisfactory in a large majority of patients. We felt that the only failures were in the early stages of our series before the most favorable combination of drugs had been established or were due to inadequate

cocainization of the pharynx and larynx. In short, no failure because of the agents, but technical failures.

RESPIRATION

Nearly all patients had a mild depression of tidal volume but usually a compensatory tachypnea so that probable minute volume remained the same. (In Chen's series, all had this phenomena.) In the early use of Demerol-Viadril, there were four apneic patients who in each case were returned to a normal respiration with a narcotic antagonist. There have also been four apneas in the Demerol-Lorfan-Viadril group; however, for different reasons. One had an obvious hyperventilation syndrome from fright; one developed oxygen apnea after jaw relaxation and subsequent obstruction and oxygen therapy; two others, however, were probably a summation of inadequate dosage of Lorfan and Viadril depression. These were promptly reversed by additional Lorfan.

Eleven patients had serious respiratory depression other than apnea, nine of which occurred prior to the concomitant use of Lorfan.

TABLE VI

BLOOD PRESSURE

Little Change	126 Patients
Rise of 20 mgm. Hg.	78 Patients 47 with insertion of laryngoscope 25 with infiltration of tonsil area (Local and Adrenaline)
Fall in O. R. of 20 mgm. Hg.	88 Patients
Recovery Room fall of 20 mgm. Hg.	75% of Patients

Table VI illustrates the changes in blood pressure experienced during the course of the anesthesia. Almost 60 per cent of the patients had a rise or fall of blood pressure while in the operating room, almost equally divided in the two categories, while 75 per cent of the patients had a decline of blood pressure in the recovery room.

This decline in blood pressure is not inconsistent with most anesthetized patients. However, in a greater number of cases, the blood pressure fell to 70 to 80 mm Hg. These patients were warm

and dry and clinically not the appearance of shock, responded sometimes poorly to vasopressors, but all spontaneously returned with wakening. This suggests a delayed autonomic blockade, but has not been of any serious concern.

Sequelae of Viadril anesthesia are shown in Table VII. As can be seen most true sequelae have to do with evidences of vein irritation. One case of hiccough persisted for about seven days, the others were transitory.

TABLE VII

UNTOWARD SEQUELAE

Headache	8
Coughing	15
Muscle irritability	8 (early series with no Demerol)
Extremities moving	23 of 45 cases without Demerol 20 of 212 cases with Demerol
Hiccough	5 cases
Vein irritation	
Thrombotic vein	10 patients
Phlebitis	10 patients
Tender vein 24 hours	25 patients

COMMENT

The use of all drugs and techniques is accompanied by sequelae, some more serious than others. With any new drugs, dosage, technique and case selection frequently vary. We believe that Viadril is an interesting drug because it is akin to drugs synthesized by our body. We believe it to be a unique sedative which produces excellent relaxation of the jaw in addition to sleep which is not common to a drug such as Pentothal. Viadril has a highly alkaline pH and as such, vein irritation is still a serious drawback. The slowness of induction may hold up a busy operating room schedule and the sleep postoperatively is often two or more hours. These disadvantages, however, have not discouraged us from using and, in fact, selecting it preferentially for many ear, nose and throat procedures.

We have administering anesthesia, interns, surgical and obstetrical residents, oral surgical residents, anesthesia residents and nurse anesthetists in addition to full time anesthesiologists. Prior to the use

of Viadril, with the same group, hardly a week went by without some frantic call for help or suspicion of imminent danger in darkened ear, nose and throat rooms with semistuperous unrelaxed patients, or apneic or unco-operative patients under local anesthesia. Since the use of Viadril, Lorfan, Demerol, this is a rare occurrence. The technique as outlined has been an evolving one which at present is 98 per cent satisfactory to patient, anesthetist and surgeon.

SUMMARY

Three hundred and twenty-five administrations of Hydroxydione are reviewed. Ninety per cent of these patients were submitted to suspension laryngoscopy, adult tonsillectomy, bronchoscopy, esophagoscopy and other procedures about the airway. Viadril, or Hydroxydione, a non-functioning steroid, is a profound sedative, lacking in analgesia but possessed of excellent jaw relaxing qualities exacting a minimal price on respiration. When coupled with topical or local anesthesia and use of narcotic drugs in small doses, it is a superior method for ear, nose and throat anesthesia in the adult from the standpoint of the patient, anesthetist and surgeon.

Slowness in onset and recovery, vein irritation and the frequent satisfactory usage of solely local anesthesia restricts this drug to procedures where topical or local alone appears to be inadequate.

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LXXXIX

THE USE OF THE FLEXIBLE FORCEPS

IN THE REMOVAL OF THE OPEN SAFETY-PIN AND OTHER BI-PRONGED FOREIGN OBJECTS FROM THE ESOPHAGUS BY GASTRIC VERSION

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Certain types of foreign bodies when they become lodged in the esophagus present a more serious problem of removal than others. Among this group are the open safety-pin and other bi-pronged objects such as staples, hair pins, large automobile upholstery tacks and bent bobby-pins with separated prongs. These objects do not present any mechanical difficulty in their removal when the points are down, which, unfortunately, is very seldom.

Of the bi-pronged foreign objects that lodge in the esophagus the open safety-pin is the one most frequently encountered, and its safe endoscopic removal, particularly in small children, offers a challenge even to the most skillful endoscopist. The most serious handicap, in these very small children, is the limitation of size of instruments that can be used and the urgent need for team-work and precision of action for the safe solution of the problem.

Jackson[1] says that there are 16 different methods by which an open safety-pin lodged in the esophagus point upward can be removed. Actually there are only a very few particularly practical and safe means: 1) by shielding the point, 2) by endogastric version, and 3) by endogastric straightening. The first and third have a very definite limitation so that the endogastric version is the most important and safe approach.

Tucker[2] devised a special forceps that when properly applied would grasp and shield the point, thereby enabling withdrawal of the safety-pin without danger of perforation. Unfortunately this technique is only possible if the safety-pin is small and the direction

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of the point is more in an upward position than lateralward, as occurs with the larger safety-pins which have stronger spring action.

Clerf[3] and others have perfected special types of forceps which, when skillfully manipulated, will close the safety-pin. The most serious handicap in the use of the above instruments in small children is the limitation in the size of instruments with which they can be used.

During the attempted removal of these objects there is the utmost need of team-work and precision of movement if one is to succeed. This is especially true when the esophagoscope is used for direct visualization of the foreign object.

Figure 1

In my personal experience the greatest difficulty in using the esophagoscope in very small children has been the marked respiratory distress produced by the displacement of the posterior tracheal wall forward. Under these circumstances any prolonged manipulation in the process of removing the foreign body may even cause the child to stop breathing. Because of this some years ago I began using a modification of the Tucker flexible forceps as a means of removing the open safety-pin and other bi-pronged foreign objects from the esophagus by doing a gastric version.

In view of its many safe and practical features I eventually adopted it as a routine procedure in the removal of these types of foreign bodies lodged in the esophagus, particularly in small children. Except for the fact that this method requires accurate fluoroscopic aid it offers many advantages over the esophagoscopic technique. The safety features are briefly:

1. It eliminates entirely the problem of respiratory distress.

2. When properly used it eliminates the possibility of traumatic perforation of the esophagus by the instrumentation itself.

3. With proper fluoroscopic aid the endoscopist can visualize every step during the process of manipulation, from the time the object is grasped in the esophagus until the version is accomplished in the stomach, and the subsequent withdrawal of the object with point trailing along the course of the esophagus.

4. Simplicity of instrumentarium in order to solve the problem.

Instrumentarium. a) flexible forceps (Fig. 1), b) good suction pump, c) metal pharyngeal aspirator to remove secretions from mouth, d) bite block to prevent the patient from biting on the flexible forceps, e) plain vaseline to lubricate the forceps.

PREPARATION OF THE PATIENT

Once the location of the foreign object has been established by x-ray, before any attempt at removal is made one should be absolutely sure that the stomach is empty of food or fluids. At least six hours should have elapsed since the last partaking of food and the contemplated time of removal of the foreign object.

In small children, in particular, where a local anesthetic is not used the proper dosage of narcotic according to Young's rule is very important to alleviate apprehension and fear on the part of the patient.

For the protection of all concerned an operative permit should always be signed by the responsible person.

PROCEDURE

Since the success of this procedure depends upon the mutual co-operation between the radiologist and the endoscopist a time suitable to both should be set.

The patient is brought directly to the x-ray department and placed on the fluoroscopic table, flat on his back in such a position that the fluoroscopic screen will be over the anatomical location of the foreign body. After proper accommodation the position of the

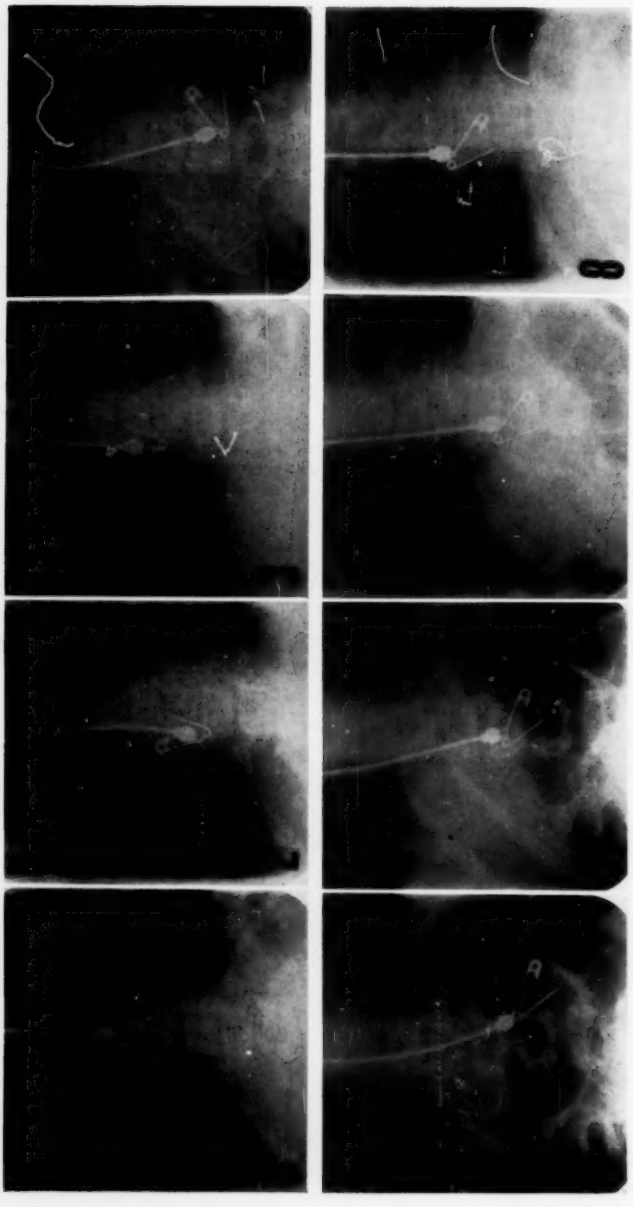

Figure 2

foreign body is re-ascertained fluoroscopically before any instrumentation is begun. This established, the patient's mouth is then held open by using the bite block and the tip of the flexible forceps (which has been lubricated with plain vaseline) is introduced into the mouth and guided gently into the pharynx and esophagus. Under fluoroscopic vision it is observed approaching the foreign object. During this stage the forceps blade itself is in the retracted position of safety within the sheath of the forceps. However, as soon as the forceps approaches the foreign body the forceps tip is advanced beyond the sheath and the forceps blades opened so that they may grasp the object. Since it is usually difficult to grasp the ring of the spring itself I prefer to grasp the shaft of the keeper. This prevents the safety-pin from slipping out of the forceps during the process of carrying out the version in the stomach, as might happen if the shaft of the point were grasped (Fig. 2).

Once the foreign body is grasped it is slowly guided into the cardia of the stomach. After the object has entered the stomach a small amount of air is introduced into the stomach from an attachment on the handle of the forceps. When the proper amount of air to slightly distend the stomach has been introduced, version of the object is gradually achieved by manipulation of the flexible forceps. When the direction of the safety-pin has been altered to that of the point trailing position, gradual withdrawal through the course of the esophagus is accomplished without any difficulty and the problem is solved.

Postoperatively the patient is kept on clear liquids for 12 hours, following which soft and regular diet may be resumed.

If any question of possible trauma exists the patient should be immediately placed on adequate antibiotic therapy and not given anything by mouth. The possibility of any serious traumatic complications can be definitely ascertained by white blood counts at four hour intervals. Any progressive rise in white blood count would be definitely indicative of possible serious complications.

Complications with the use of this technique are extremely rare and I have not had any in my series of cases. Needless to say the success of this technique not only depends on the ability and training of the endoscopist but just as equally upon the proper radiological aid given during the process of fluoroscopic visualization.

I would like to report briefly three of the earliest cases which led me to adopt this technique, when attempts at esophagoscopic

removal of foreign objects had been unsuccessful. Since then I have used this method exclusively, particularly in small children.

REPORT OF CASES

CASE 1. J.W., a twelve month old white male, was admitted to Mt. Sinai Hospital on February 8, 1944, for removal of an open safety-pin which was lodged in the lower thoracic esophagus. Two previous attempts at removal by another endoscopist in a different hospital had not been successful because of the marked respiratory distress that occurred on each occasion which forced discontinuance of the procedure. This was understandable in view of the child's marked under-development. Because of the previous experiences it was thought advisable to try the use of the flexible forceps instead of esophagoscopy.

On February 9, 1944, under fluoroscopic vision, the flexible forceps with a ring rotation blade, was advanced to the upper end of the safety-pin at which time the blades were opened wide. At first, grasping of the ring portion of the spring of the safety-pin was attempted but since this was unsuccessful the shaft of the keeper was grasped and the safety-pin was then advanced into the stomach. At this point the stomach was distended slightly by insufflating some air by means of a bulb attached to the small insufflating canal on the side of the forceps handle. By manipulation of the flexible forceps the gradual rotation of the safety-pin could be followed under fluoroscopic view. Once complete version of the safety-pin was achieved withdrawal through the esophagus with the point trailing became a very simple matter and the foreign body was retrieved.

Throughout the entire procedure this infant had no respiratory distress whatsoever. The entire procedure took about 12 minutes. The child was discharged from the hospital on February 11, 1944, without any complications.

CASE 2. M.T., white male infant, five weeks of age, was one of the early patients in which this technique was used. This infant had first been admitted to St. Luke's Hospital in Philadelphia on July 9, 1945, because of sudden onset of dyspnea and cyanosis thought to be due to a convulsion. After recovery from the convulsion, because of persistence of dyspnea, an x-ray of the chest was made which revealed a surprising finding, namely, a bent bobby-pin lodged in the upper thoracic esophagus and another straight one in the stomach.

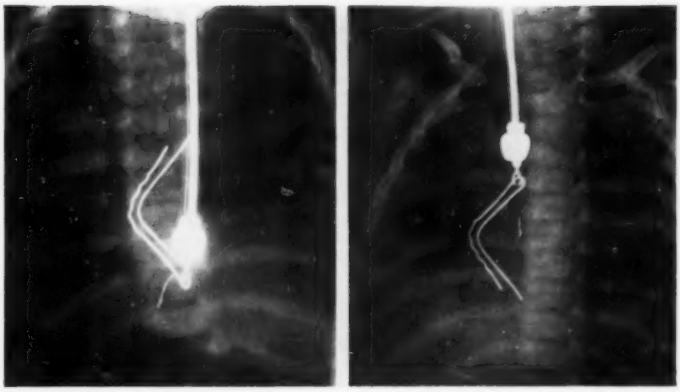

Figure 3

The infant was transferred to Mt. Sinai Hospital in Philadelphia on July 10, 1945, and admitted on my service for removal of the bobby-pin from the esophagus.

Several attempts to remove it by esophagoscopy failed, since it was impossible to bring the two points of the bobby-pin together because of their firm separation. In desperation it was decided to resort to the use of the flexible forceps, using a ring rotation blade in order to facilitate doing a gastric version of the object if it could be grasped at its lower end.

Under fluoroscopic guidance the tip of the forceps was advanced to close proximity of the lower end of the bobby-pin, at which time the forceps blades were opened wide and after some maneuvering the lower curve of the bobby-pin was grasped (Fig. 3). Once this was accomplished the object was carried into the stomach. After inflating the stomach with air, version of the bobby-pin was accomplished under fluoroscopic vision. After the version, the withdrawal through the esophagus was uneventful and the foreign object was retrieved. The entire procedure took about ten minutes and fluoroscopic aid was only used intermittently for only a fraction of this time.

The other bobby-pin that was originally in the stomach had by this time passed into the distal portion of the duodenum, from which it was removed by laparotomy on July 16, 1945. In spite of

all these procedures the child was discharged from the hospital completely recovered on August 4, 1945.

Case 3 is reported because of its illustration of the adaptability of the flexible forceps technique in the solution of this difficult problem.

Case 3. C.R., white female, 12 months of age, was admitted to Abington Memorial Hospital on June 2, 1945, with history that her parent had seen her swallow an unusually large open safety-pin. Attempt by her parent to retrieve it by putting the finger back into the throat had failed.

On x-ray examination a large open safety-pin with a wide spread could be clearly seen in the region of the mid-thoracic esophagus.

Because of the very large size of the safety-pin and the width of the open prongs I feared that difficulty would be encountered in trying to carry out a version in the stomach of this small child. Since there was no alternative the flexible forceps technique of removal was decided upon. Because of the interference by the large keeper to allow the advance of the flexible forceps tip in a straight line, it was impossible to grasp the ring of the spring with the rotation forceps blades so that we had to be satisfied to grasp the shaft of the keeper. Once this was accomplished we were able to advance the pin into the stomach, but in spite of the fact that the stomach was well distended the safety-pin did not appear to have freedom to rotate. At this point I learned a very important lesson in the use of this technique to avoid losing the foreign body during the process of doing the version. During the manipulation of the forceps the blades began to slide towards the keeper end and I am sure that if I had grasped the shaft of the point I would have lost the safety-pin and there would not have been any hindrance to keep the blades from sliding off the end. By further manipulation it was possible to advance the blades down to the region of the spring again and gradual version was then accomplished and the safety-pin successfully removed. This was one of the longest procedures, lasting 18 minutes.

This child was discharged on June 4, 1945, without any complication.

In spite of the tense moments associated with the removal of this foreign object it offered a very practical lesson in the successful

solution of these serious problems, namely, when it is impossible to grasp the ring of the spring always grasp the shaft of the keeper so as to avoid having the foreign object slip off from the forceps blade during the process of doing the version, as might happen if the shaft of the point is grasped.

CONCLUSION

1. Because of its safety and practicality, in the last 14 years I have used the flexible forceps technique exclusively in the removal of the open safety-pin and other bi-pronged objects that have become lodged point up in the esophagus proper below the level of the cricopharyngeus.

2. This method has been used on over 50 small children for removal of the open safety-pin and other types of bi-pronged foreign objects lodged in the esophagus proper without any complications, except that in two cases the safety-pin slipped off the forceps into the stomach while doing the version. In both cases they were retrieved.

3. One of the greatest advantages in its use is that it eliminates the factor of respiratory distress, so often encountered in small children with the technique of esophagoscopy.

4. The use of the wide expanding ring rotation type of blades in the flexible forceps is of the utmost importance, so as to be able to carry out version of the foreign object in the stomach.

5. The reason for not having reported this method sooner was the fact that I took it for granted that others were using it also, until recently when I found out otherwise.

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XC

EVALUATION OF PHOTOGRAPHIC METHODS IN THE ENDOSCOPIC STUDY OF THE AIR AND FOOD PASSAGES

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The principal types of apparatus available for endoscopic photography at the present time are the Holinger-Brubaker type[1] (Fig. 1) using co-axial lighting through an open tube, and the French type developed by Fourestier, Gladu and Vulmière[2] (Fig. 2), with the co-operation of the French government, which uses a quartz rod to transmit light from a proximal source. There are advantages and disadvantages to both systems. No better pictures will ever be taken than those taken by Holinger, but the large endoscopic tubes necessary limit the procedure somewhat, and besides, the apparatus is heavy to hold. The French type of apparatus uses tubes of the regular size, and hence can be used more routinely or, to use the word of Max Fourestier, "universally." Almost any still or motion picture camera can be used with the quartz rod-lighted endoscopes, provided a simple adapter is used to steady the camera rigidly in relation to the telescope, and center the image. Of course, reflex-type cameras are much better than others, and they are less wasteful of film.

The "fotobronchoscope" (Fig. 3) has been described previously and repetition of the description seems unnecessary, but I wish to state that the most meticulous care in manufacture and assemblage of all the optical parts is absolutely indispensable, as is also the most scrupulous care of the instrument. The lenses used in our luminator are imported from France; and the quartz rods are imported from Germany, though prepared and mounted here, in strict accordance with the specifications of the Institut d'Optique in Paris and under license of the C.N.R.S. (or Centre National de Recherche Scientifique).

STILL PHOTOGRAPHY

As previously stated, cameras with reflex finders are generally preferable, though others may be used. We have found the Alpa

From the Chevalier Jackson Clinic, Temple University Medical Center, Philadelphia.

Reflex (Fig. 4) especially convenient, with an f 3.5 38 mm Alfinar lens, though there are a number of other suitable reflex cameras on the market. Though not a reflex without use of auxiliary parts, the Robot has the advantages of great lightness and automatic film transport, which makes it possible to take several shots in quick succession, without rewinding. The Robot we have used is equipped with a Schneider Xenar f 2.8 38 mm lens. There are those who say that we shall never be able to get really good stills in color without the use of flash, but with the faster and faster color films coming out, I am still hopeful that pictures made without flash will eventually prove satisfactory. We have experimented with regular Anscochrome, developing it at 64, and also with Super Anscochrome Tungsten and Super Anscochrome Daylight type film. The last appears best at the present time, and acceptable pictures may be obtained at 1/25 and even 1/50 of a second, whereas with Kodachrome 1/10 sec. seems to be necessary.

CINEMATOGRAPHY

While many people are unwilling even to consider the use of 8 mm film, it has several features to recommend it. Of course, economy is obviously one advantage, though perhaps not a very important one. Secondly, there is the great convenience of using a compact, lightweight little camera like the French Camex Reflex (Fig. 5), which is easy to handle and gives a beautiful big, bright, sharp image all the time that you are filming. Only Kodachrome A has been used for 8 mm pictures, because so far it is the only film available in that size. The pictures obtained are excellent for showing in any room of moderate size. The disadvantages are, first of all, that 8 mm film is not so easy to work with, splicing, editing, etc., and secondly, that provision is not generally made for good 8 mm projection at meetings. Since 16 mm film is standard, you will find repeatedly that you want to splice endoscopic footage into other 16 mm films. Why not enlarge the 8 mm film to 16 mm? The laboratories doing this work are few and they generally take an unreasonably long time to do the job. Most important, the results have not done justice to the quality of the 8 mm film, in our experience. Though certainly for one's own records routine filming on 8 mm film such as practiced by Dubois de Montreynaud[8] and his colleagues in Reims has its merits, routine 16 mm cinematography will probably be preferred by the majority of endoscopists in the United States.

For 16 mm cinematography we have found the Pathé Webo (Fig. 6) equipped with a pistol grip and trigger release the most

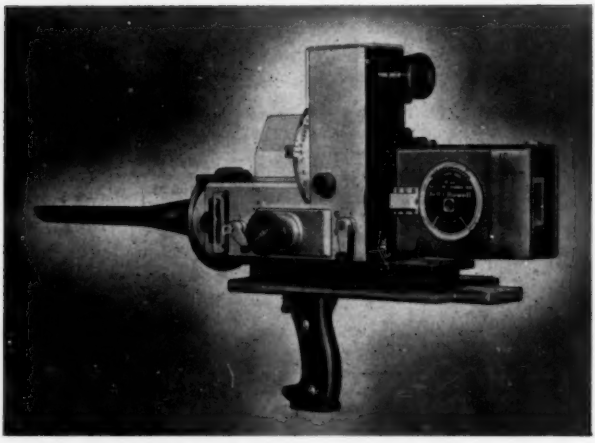

Fig. 1.—Holinger-Brubaker endoscopic motion picture camera (Bremo I). This camera uses a Bell & Howell magazine camera box, with a 90 mm f 4.5 Wollensak Raptar Series II lens. A number of different sizes of endoscopes can be used with this camera.

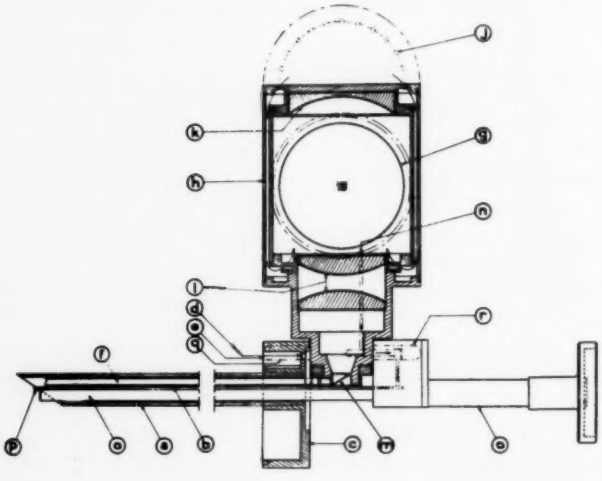

Fig. 2.—Diagram of the optical system of the French quartz rod type of apparatus developed by Fourestier, Gladu and Vulmière. This same optical system is used in our Pilling-made Fotobronchoscope, for which the lenses are imported from France and the quartz from Germany.

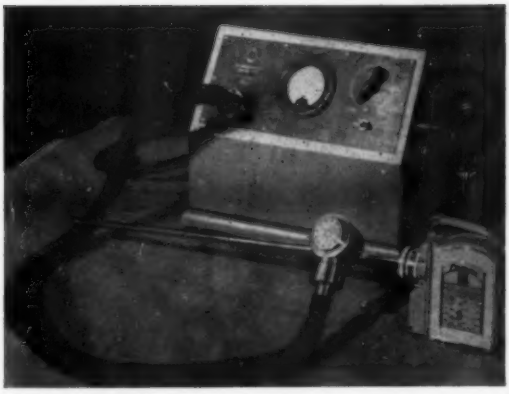

Fig. 3.—The Jackson-Pilling Fotobronchoscope with Camex Reflex (8 mm) camera attached, showing Pilling unit which contains rheostat and also blowers for negative pressure used in cooling, and positive pressure used for anti-fogging device.

satisfactory camera; it balances well, is not too heavy, and has a reflex finder giving a fairly bright and fair-sized image; furthermore, though spring wound, it has a long run with each rewinding. We have used a Cinor Berthiot f 1.9 20 mm lens. We have also used experimentally a retrofocus Angénieux f 2.2 12.5 mm which gave a bright and sharp, but too much smaller, picture. As for film, we have used mostly Kodachrome A, but recently have tried Super Anscochrome Daylight type (No. 225) with very gratifying results. The extra emulsion speed allows the camera to be run at 24 frames per second if desired.

Other cameras we have used are the Bolex Reflex (Fig. 7) and the Arriflex. These cameras are, of course, excellent, but the Bolex gives a smaller and dimmer reflex image than the Pathé, and the camera is much heavier. For the Bolex Reflex, a dual power viewer is made by Pellegrini-Piek of San Francisco which can be installed for $60 and this gives a much brighter and larger image. Cameras not of reflex type may be used, but the reflex finder is really even more important for cinematography than for still pictures, and there is no doubt that the prefernce for cameras so equipped is well-founded.

Just as the Holinger-Brubaker type of apparatus can be adapted for use in the larynx and esophagus as well as in the tracheobronchial

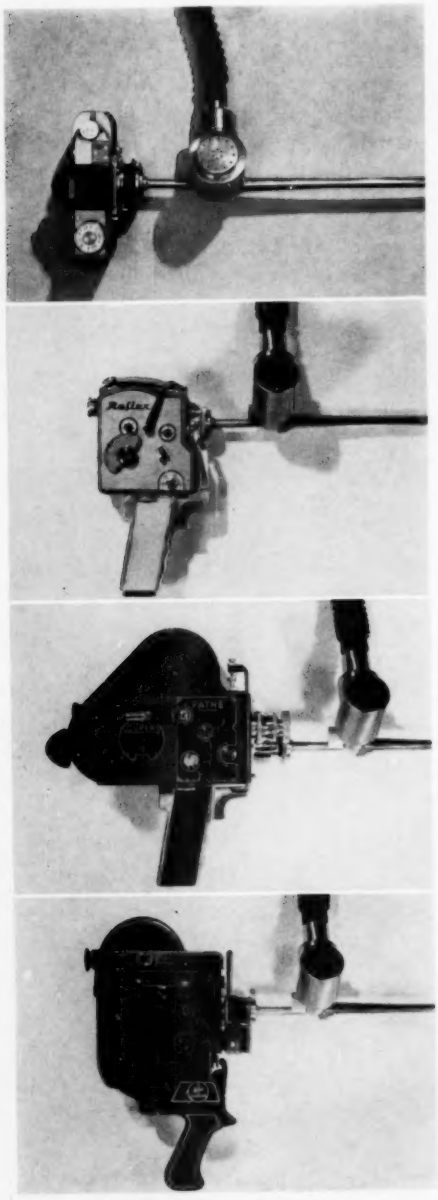
Reflex
PATHE

Fig. 4.—Fotobronchoscope with Alpa Reflex (Swiss) attached, for taking stills. Any other camera can be used, but the lens must focus sharply at 2 feet (50 cm) and cameras of reflex type are to be preferred.

Fig. 5.—Fotobronchoscope with Camex Reflex 8 mm (French) attached. Note that this and cameras shown in Figures 6 and 7 have pistol grip handles attached, with trigger release.

Fig. 6.—Fotobronchoscope with Pathé Webo 16 mm (French) attached. This camera has proven especially satisfactory for endoscopic work.

Fig. 7.—The Bolex Reflex 16 mm (Swiss) is quite satisfactory for endoscopic work, especially if equipped with the dual power viewer made by Pellegrini-Piek of San Francisco.

tree, so can the quartz-rod type. First efforts at photography of the larynx with this type of apparatus were made by Vallancien[4] of Paris, and first uses of a quartz-rod esophagoscope were reported by Ségal[5] of Reims and by Aubin[6] of Paris. A very ingenious and cleverly designed truly "universal" instrument was presented recently by Rose.[7] This instrument is self-contained and can be passed through almost any endoscope. It can be used for either movies or stills and for the latter a flash is used.

Finally, a few words about the value of endoscopic photography as we see it today. The first endoscopic pictures were viewed with great interest, though more or less as a novel feat of scientific accomplishment; but now the photographic method has opened up new promises of more accurate records in clinics where this method is used routinely as in Reims, and better opportunities for practical consultation and conference study of the problem case, to say nothing of more realistic undergraduate and postgraduate teaching. Holinger's[8] "Atlas" (1951) presented the finest collection of graphic representations of the appearances of laryngeal disease ever seen. Study of the normal anatomy of the tracheobronchial tree and its variations, as well as study of neoplastic, tuberculous and other lesions of the accessible bronchi, can now be carried out not only by the individual endoscopist but by the Chest Conference group. I feel that we should continue to work on the development of photographic apparatus and techniques, and endeavor to illustrate our case records with as much good photographic material as possible, including both still and motion pictures, preferably in color! As shown by Soulas[9] the bronchoscope universal or fotobronchoscope photography may be used in connection with television.

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XCI

ACUTE OBSTRUCTING BRONCHIOLITIS: A MEDICAL EMERGENCY

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In 1951, Cardon, Lemberg, and Greenebaum[1] very ably described the effects of acute bronchitis and bronchiolitis occurring in patients with chronic asthmatic bronchitis, emphysema, and pulmonary fibrosis. They called attention to the severe obstructing effect of secretions in such circumstances, often leading to acute respiratory failure and death by suffocation. Prior[2] in the following year called attention to the same type of acute respiratory emergency. Often the disease described so clearly by these authors fails to be recognized early enough in its course to respond to appropriate treatment. Because effective treatment does exist, principally bronchoscopic aspiration of the drowned tracheobronchial tree, further description of the disease and its treatment seems indicated.

This paper consists of four major topics: the anatomical, physiological, and pathological aspects of acute obstructing bronchiolitis; the clinical features of the syndrome; its treatment based upon experience derived from the management of seven adults with this disease; and a final section dealing with the details of bronchoscopic aspiration.

ANATOMICAL, PHYSIOLOGICAL, AND PATHOLOGIC FEATURES OF ACUTE OBSTRUCTING BRONCHIOLITIS

Certain alterations of pulmonary structure and function are necessary for the occurrence of acute obstructing bronchiolitis.

The first and most important abnormality is obstruction to airflow in small airways. There are a number of mechanisms whereby such obstruction can occur. Some are illustrated in Figure 1. Of

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these, bronchospasm is widely appreciated by most physicians. An equally important mechanism of obstruction to airflow is excessive thick secretions, consisting of a mixture of mucosal glandular products and of inflammatory exudate. Loss of airway support due to disruption and deformity of neighboring parenchyma, though not generally correctible by known methods of treatment, is another significant obstructing factor. It has been aptly characterized by Wright and Filley[3] as loss of the "guy wires" supporting the airways. Thickening of membrane lining the airways with encroachment upon the lumen is a known pathologic finding in patients with chronic bronchopulmonary diseases, and frequently sets the stage for the development of obstructing bronchiolitis. The last mechanism of obstruction represented in Figure 1, that of compression of the airway by contiguous engorged pulmonary vessels, probably exists in the illness called cardiac asthma. An additional mechanism of obstruction not illustrated in Figure 1 is that of distortion or kinking of airways which will be discussed in a later paragraph. Last to be mentioned is that form of obstructing mechanism discussed by Prior[2] who describes an inflammatory granuloma projecting into the lumen of the airway offering resistance to flow of air. Whereas any one of the above mentioned mechanisms conceivably could lead to critical impairment of ventilation, it seems more reasonable to suspect a combination of mechanisms operating simultaneously in the syndrome of acute obstructing bronchiolitis.

Second in the consideration of underlying pulmonary abnormalities responsible for acute obstructing bronchiolitis is the factor of bronchiectasis. This condition can be illustrated simply in Figure 2. Here the pleural surface is represented by an outer circle. The airway with its ciliated mucous membrane and spirally oriented layer of smooth muscle is located within the outer circle. The support therein is indicated by spring-like lines representing elastic parenchyma intervening between airway and pleura. When severe injury to the bronchial wall occurs, and healing ensues by replacement with scar tissue, the dynamic muscle tissue is lost in a given segment of the airway. Under the continuous dilating force of elastic parenchyma the scar becomes thin by stretching. Cilia, if present, become more widely separated and less effective in maintaining the continuity of the mucous conveyor belt. Secretions than collect in the outpouchings, particularly when they are dependent. Secretions so collected can be aspirated into more peripheral sites within the airways and thus contribute to the genesis of acute obstructing bronchiolitis.

In Figure 3 are shown in simplified form further structural changes in chronic bronchopulmonary diseases. In the left upper

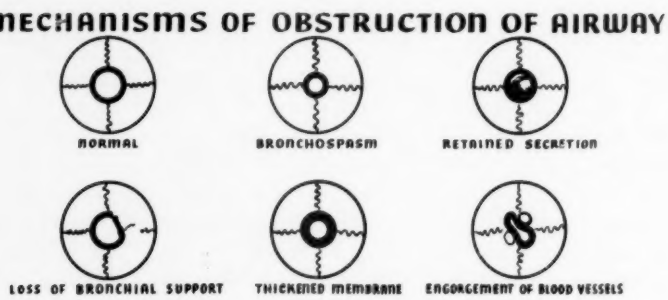

Fig. 1.—Diagrammatic illustration of some of the mechanisms of obstruction to airflow in the lungs of patients with obstructing disease of airways. Pleura is represented by an outer circle, airway by the inner circular structure and parenchyma by spring-like lines.

corner of the figure is represented a bronchiole and some of its branches leading to primary lobules, i.e., respiratory bronchioles and their associated alveoli. On the right in the figure, two of the lobules have been obstructed by intrinsic plugs. The results of this obstruction consist of atelectasis of the affected primary lobules and compensatory hyperinflation of the neighboring lobules. When two adjoining lobules become atelectatic, the enforced displacement of a nearby lobule could lead to kinking of the airway supplying that lobule. An additional mechanism of airway obstruction is thereby depicted and named kinking. Were infection to supervene, the obstructed atelectatic lobules could be destroyed with consequent fibrosis. In the lower diagram of Figure 3 are shown further possible changes. If obstruction of flap-valve type were to exist in the kinked airway, an air cyst could form and compress the lobule next to it. The result of the combined changes is rather impressive. Five normal lobules are converted into three atelectatic functionless units, one cyst, and one remaining lobule capable of function, itself relatively hyperinflated.

Along with the lobular changes illustrated, alterations in associated pulmonary vessels must occur. In the case of atelectatic fibrosed lobules the vessels involved in the scarred remains of parenchyma could be occluded. In the cystic lobules stretching and flattening of vessels also could lead to obstruction to blood flow. Safely one could say that loss of functioning air spaces is accompanied by loss of functioning vasculature. When loss of vessels reaches critical

proportions, increased pulmonary vascular resistance obtains, and with it pulmonary hypertension. Later in the course of events, cor pulmonale becomes a reality. The chain of events as described is recapitulated in the list below:

Lobular obstruction

Lobular atelectasis

Lobular fibrosis if infection supervenes

Compensatory hyperinflation of neighboring lobules

Distortion of airways (kinking)

Cyst formation

Compression by cysts of neighboring lobules

Increased pulmonary vascular resistance

Pulmonary insufficiency

With the addition of acute infection or irritation which produce exudation and hypersecretion the results are: lobular drowning in exudate, inflammatory thickening of alveolar-capillary membrane, and further increase in pulmonary vascular resistance due to vasospastic reflexes in hypoxic lobules. The final pulmonary problem then becomes: critically diminished alveolar ventilation, impaired alveolar capillary diffusion, pulmonary hypertension, cor pulmonale, critically diminished tussive force, accumulation of secretions not only in smaller airways but also in major airways, arterial oxygen deficiency, excessive accumulation of carbon dioxide, and respiratory acidosis.

THE CLINICAL SYNDROME OF ACUTE OBSTRUCTING BRONCHIOLITIS

There are certain groups of patients in whom acute obstructing bronchiolitis occurs. It is said to be a disease of the extremes of age.[2] Infants under three[4] are commonly observed with acute respiratory illnesses named bronchiolitis. It is possible that the reason for the predisposition in infancy lies in the fact that the lungs of infants are relatively unexpanded in the early years of life. Thus airways remain relatively small and easily obstructed. Sometimes the disease is observed in postoperative patients. Here the predisposition could lie in poor thoracopulmonary expansion. Often the disease appears in

TABLE I — OBSTRUCTING BRONCHIOLITIS, CLINICAL DATA

	SEX	AGE	DIAGNOSES	B.P. MM HG.	TEMP. °F	PULSE PER MIN.	INFECTING ORGANISM	WBC PER MM^3	HB. GM %	PCV %	CO_2 MEQ.	ART. SAT.		
1.	F	60	Asthmatic Bronchitis Ca. Breast	110/78	100°	90	Alpha Strep. Neisseria	22,350	10.6	33	37.5	77.3%	Tracheostomy	Recovered
2.	M	56	Emphysema Fibrosis Polycythemia Cor Pulmonale	125/80	98.6°	100	N. Catarrhalis Gamma Strep.	8,800	17.7	61	38.9		Bronchoscopy	Recovered
3.	F	63	Emphysema Asthmatic Bronchitis Rheumatic Heart Disease Cong. Failure	120/70	99°	104		17,300	17.7	60	44.9	78.1%	Bronchoscopy	Recovered
4.	F	77	ASHD* Cong. Failure Asthmatic Bronchitis	130/80	99.4°	92	Pseudomonas E. Coli	14,700	12.7	41	38.7		Bronchoscopy	Recovered
5.	F	64	Asthmatic Bronchitis Smoker's Lung	130/70	98.6°	110	Micrococcus (Coag. Pos.) Neisseria	17,300	15.9	49	32.4		Bronchoscopy	Recovered
6.	M	66	Emphysema Asthmatic Bronchitis	126/76	100.6°	123	Strep. Fecalis	32,325	17.3	52	26.3		Bronchoscopy	Recovered
7.	F	47	Emphysema Asthmatic Bronchitis	115/60	100.6°	130	Alpha Strep.	15,300	12.9	53	—		Bronchoscopy	Recovered

* Arteriosclerotic Heart Disease

the presence of congestive heart failure, a situation in which edema of airways and compression by engorged vessels contribute to airway obstruction. In the seven cases summarized in Table I, a chronic respiratory illness characterized by obstruction of small airways existed, to which two or more of the following names could be applied: chronic bronchitis, smoker's lung, asthmatic bronchitis, emphysema, and pulmonary fibrosis. Bronchiectasis and cystic disease are also two predisposing conditions.

Symptoms and signs of acute obstructing bronchiolitis can be described under the following headings: general, respiratory, circulatory, and central nervous.

Certain general manifestations are present in most patients with acute bronchiolitis. Often an acute respiratory illness, a cold, can be identified in the history immediately preceding onset. Rapid progression is emphasized by Cardon, et al,[1] and can be exemplified by the following report:

A 66 year old railroad worker (Case 6, Table I), previously treated for emphysema and chronic bronchitis, was seen one evening at 10:00 p.m. in the hospital emergency room for moderate dyspnea of one hour's duration. The symptoms responded to inhalation of nebulized isopropyl arterenol, and the patient returned to his home. At 7:00 the following morning he was admitted to the hospital in coma with a rapid irregular cardiac rhythm at a rate of over 120 beats per minute, gross cyanosis, markedly poor breath sounds, absence of wheezes, poor minute volume of ventilation, and intercostal retraction during inspiration. Bronchoscopy revealed copious mucopurulent secretions filling the tracheobronchial tree to the level of the carina. After adequate aspiration and other means of therapy the patient recovered with residual subtotal amblyopia considered due to prolonged hypoxia.

An insidious onset is also illustrated by the report of the following patient:

A 60 year old white woman (Case 1, Table I) underwent a right radical mastectomy for carcinoma of the breast after a week of preoperative therapy for emphysema and chronic bronchitis. During the postoperative period complicated by minimal right pneumothorax, subcutaneous emphysema, and excessive bronchial secretions, the patient developed progressive dyspnea requiring five days for the occurrence of alarming ventilatory obstruction. This responded to trache-

ostomy and periodic removal of secretions, plus other therapeutic measures.

In patients with acute obstructing bronchiolitis the febrile reaction is generally mild, if present. The lack of fever is inconsistent with the gravity of the illness.

Respiratory manifestations are most significant and consist of an ineffective wet cough and the raising of sticky colored sputum, when and if sputum is raised. Gurgling râles ordinarily are present and indicate failure of adequate clearing of airways. Auscultation of the chest yields the most diagnostic evidence for the existence of acute obstructing bronchiolitis. Extremely poor inspiratory breath sounds in combination with a relatively silent prolonged expiratory phase of respiration can be detected with ease. It is believed by the authors that airflow is so poor in these patients that wheezes may be minimal or absent. The most important feature, thus, is a disproportionately low minute volume of ventilation despite distinctly increased respiratory efforts. Needless to say, cyanosis is striking.

Circulatory symptoms command careful attention. Often at first glance the patient appears to be suffering primarily from acute congestive cardiac failure with rapid irregular cardiac rhythm, distended peripheral veins, ankle edema, and sometimes hypotension of variable degree. Characteristic of acute obstructing bronchiolitis are a loud pulmonic second tone, when and if cardiac tones are audible, and pulsus paradoxicus. The latter finding is often quite remarkable and is undoubtedly the result of restricted cardiac output from diminished central volume due to prolonged expiration at relatively high positive intrathoracic pressure.

Central nervous manifestations of acute obstructing bronchiolitis include depression and irritability characteristic of hypoxia, progressing to delirium, stupor, and coma. When retention of carbon dioxide supervenes, decrease in rate and depth of respiratory efforts can become severe. The illness then becomes self-propelled toward fatal termination unless prompt efforts are expended in the patient's behalf.

In the laboratory certain findings are worthy of comment. Leukocytosis is the rule in this disorder, although not necessarily at the immediate onset. In the seven patients herein under consideration, leukocytes numbered from less than ten to thirty thousand. Sputum examinations disclosed variable bacterial flora. Carbon dioxide reten-

tion was looked for and found in six of the seven cases, and arterial oxygen deficiency was severe in the two patients from whom arterial blood samples were obtained. Thoracic roentgenograms yielded no characteristic abnormalities except findings indicative of pulmonary hyperinflation.

Outstanding in the differential diagnosis of acute obstructing bronchiolitis is the need for recognizing its presence even when apparent good evidence for acute congestive cardiac failure exists. Because of rapid irregular pulse, ankle edema, dyspnea, cyanosis, and gurgling inspiratory râles, the patient with acute obstructing bronchiolitis sometimes is treated for congestive cardiac failure with pulmonary edema. Whereas it is not uncommon for acute obstructing bronchiolitis and cor pulmonale with ankle edema to exist together, it is not possible to effect improvement in the patient without directing vigorous therapy toward the lungs. Obstructing bronchiolitis is clearly recognizable by a finding of great importance — strikingly poor minute volume of ventilation. In pulmonary edema the rule is a high respiratory minute volume. Status asthmaticus attracts attention in differential diagnosis. Because of critically impaired minute volume of ventilation, the typical patient with obstructing bronchiolitis is usually incapable of generating wheezes. Furthermore, obstructing bronchiolitis is characterized by carbon dioxide retention, arterial oxygen deficiency, and infection, while status asthmaticus is not considered by the authors to be a permissible diagnosis when infection and carbon dioxide retention exist and when wheezes are not prominent.

TREATMENT

Fundamental aims in the treatment of acute obstructing bronchiolitis include the following. First is the removal of secretions already formed. Since the disorder is characterized by gross obstruction to airflow, tussive force is necessarily very poor. Secretions which accumulate in the small airways eventually enter major airways wherefrom they are aspirated during each inspiration into more distal smaller airways if they are not promptly removed. For this reason, any technique by which material in the larger airways can be removed must be employed without delay. The second aim in therapy is the prevention of further formation of secretions and exudate, best accomplished by prompt use of anti-inflammatory agents, namely, antibiotics and adrenal corticosteroids. A third and final aim is the restoration of adequate alveolar ventilation.

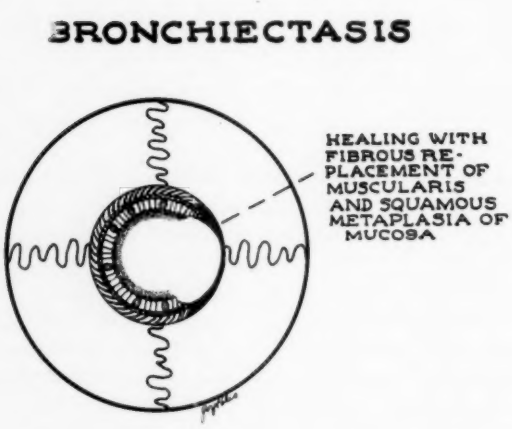

Fig. 2.—Schematic representation of bronchiectatic changes. Pleura is depicted by an outer large circle, airway by the inner circular structure, and intervening elastic parenchyma by the spring-like lines.

In detail, the removal of secretions from the airways in obstructing bronchiolitis is accomplished in a stepwise fashion. An inhaled nebulized bronchodilator constitutes the first and simplest maneuver. When bronchospasm exists, a bronchodilator can be expected to improve airflow and thus tussive force, thereby aiding the patient in clearing his own airways by coughing. In the type of patient herein described, however, the administration of an inhaled nebulized bronchodilator is inadequate. Whereas Cardon[5] has described cleansing of the airways by means of suction through a rubber catheter, introduced into the trachea, this method is ordinarly inadequate because the technique does not permit of systematic cleansing in airways under direct visualization. Tracheotomy renders repeated suctioning of airways simple, but it too lacks the desirable feature of direct visualization inherent in skillful bronchoscopy. This latter technique will be described in detail in a subsequent section. It has been utilized successfully by Fearon and Bain[6] in the treatment of children with acute bronchiolitis.

Because of the inflammatory origin of obstruction in obstructing bronchiolitis, antibiotics and adrenal corticosteroid hormones are extremely useful. Antibiotics in large therapeutic doses are given promptly. For example, daily doses of two grams of tetracycline were used most commonly in the seven patients treated by the authors

of this paper. Cultures of sputums with antibiotic sensitivity studies of the isolated organisms led to alterations in the drugs employed in some instances. In view of the life-threatening gravity of obstructing bronchiolitis, concern about the disadvantages of adrenal corticosteroid therapy is not warranted. Such drugs administered on the basis of acute emergency can be stopped, should possible complications exceed the advantages gained from their use. In our own experience with patients in mild congestive failure allegedly due to cor pulmonale, a gratifying diuresis rather than fluid retention occurred. As a concrete example of our habits of treatment, we usually give the patient with acute obstructive bronchiolitis prednisone in a dose of 15 mg every six hours, or triamcinolone 12 mg every six hours, subsequently tapering the dose. Important to bear in mind is the fact that any improvement in the airflow to hypoxic lobules leads to higher pressure of oxygen in alveoli, thereby reducing locally increased pulmonary vascular resistance. This reduction in reversible resistance can be of aid in ameliorating cor pulmonale.

In patients with obstructing bronchiolitis, an outstanding difficulty is inadequate alveolar ventilation resulting in arterial oxygen deficiency and retention of carbon dioxide. Exhaustion caused by increased resistance to airflow and asphyxia can lead to failure of respiratory drive. Since muscular activity, i.e., exercise, is one of the most powerful stimuli to respiration, bed rest can be detrimental as demonstrated in the following example:

A 56 year old white man (Case 2, Table I), previously treated for severe pulmonary emphysema and chronic bronchitis, sustained a cold and thereafter developed increasing dyspnea and cough associated with ankle edema of three weeks' duration. Examination disclosed cyanosis, plethora, hyperinflation of the thorax, grossly decreased inspiratory breath sounds and prolonged faint expiratory wheezing breath sounds. In addition, pitting edema of moderate degree extended to the knees.

The patient was admitted to the hospital and placed at bed rest. One hour after being put to bed the patient's rate and depth of respiration decreased remarkably and he became difficult to arouse. Cyanosis became extreme. Passive motion of extremities resulted in distinct increase in depth and rate of respiration. Following bronchoscopic aspiration with removal of large volumes of mucopurulent secretions, the patient was purposely kept awake. Rate and depth of respiration were maintained by repeated changes in position, passive motion of extremities, dangling, standing, and brief walks about his bed.

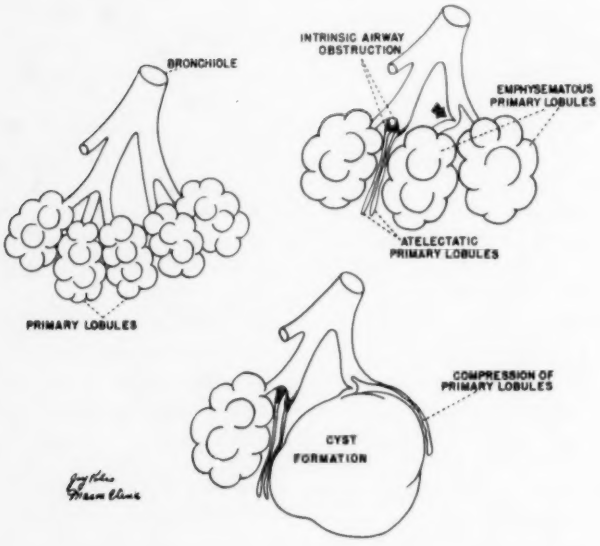

Fig. 3.—Diagrams of some of the changes in airways and pulmonary parenchyma resulting from obstruction of small airways. In the left upper corner of the figure is represented a bronchiole with some of its branches leading to primary lobules, i.e., respiratory bronchioles and their associated alveoli. On the right in the figure, two of the lobules have been obstructed by intrinsic plugs. The results of this obstruction consist of atelectasis of the affected primary lobules and compensatory hyperinflation of the neighboring lobules. When two adjoining lobules become atelectatic, the enforced displacement of a nearby lobule could lead to kinking of the airway supplying that lobule. An additional mechanism of airway obstruction is thereby depicted and named kinking. Were infection to supervene, the obstructed atelectatic lobules could be destroyed with consequent fibrosis. In the lower diagram of the figure are shown further possible changes. If obstruction of flap-valve type were to exist in the kinked airway, an air cyst could form and compress the lobule next to it. The result of the combined changes is rather impressive. Five normal lobules are converted into three atelectatic functionless units, one cyst, and one remaining lobule capable of function, itself relatively hyperinflated.

Following the removal of secretions by aspiration and the administration of anti-inflammatory agents, the maintenance of adequate alveolar ventilation sometimes demands mechanical aids. The various apparatuses which produce intermittent inspiratory positive pressures can be very useful, e.g., the Bennett valve. The authors use this type of apparatus in all patients with obstructing bronchiolitis. The concomitant use of an inhaled bronchodilator nebulized by the IPPB

apparatus adds to the effectiveness of the treatment. Additional aids to ventilation include tank respirators.

Often heart failure of left ventricular type coexists with obstructing bronchiolitis. In fact, it has been pointed out that congestive failure with pulmonary edema sometimes appears to be the outstanding feature of the ill patient. The cardiac problem must be treated appropriately with sodium restriction, diuresis and digitalization. But distinctly important is the fact that the obstructed ventilation must be corrected to attain therapeutic success.

BRONCHOSCOPIC ASPIRATION

The purpose of bronchoscopy is four-fold. The first is diagnostic to determine the state of the tracheobronchial tree, the amount of edema, inflammation and secretions. The second major purpose is to remove the excessive secretions. This is done very slowly allowing sufficient time for further secretions to drain from the alveoli into the bronchus for as complete removal as is possible. To aid this it is found useful to instill a vasoconstrictor into the tracheobronchial tree. The favorite in use by this group is ¼ per cent neosynephrine. After the secretions are initially thoroughly removed, a few drops of neosynephrine are passed through the scope and the bronchi are observed for mucosal blanching and dilatation. This again permits more complete suction throughout the tracheobronchial tree.

As discussed above, one of the major problems in these patients is the lack of cough reflex resulting from debility. For this reason it is felt that bronchoscopy should also attempt to stimulate cough reflex. Though it would appear to be traumatizing to the patient, anesthesia for this reason is avoided whenever possible. Local anesthesia to the tracheobronchial tree will obtund the cough reflex for several hours and very often the therapeutic effect of endoscopy is lost when such an anesthetic agent is used.

For the actual mechanics of bronchoscopy the patient is usually left in bed as any transport usually results in further anoxia and cardiac load. The semi-Fowler position has been found most convenient by this group as this makes it very easy for the examiner diagnostically, as well as leaving the patient in an upright position for instillation of vasoconstrictors. If anesthetic solution is required, the transtracheal technique is employed as this requires the least manipulation of the patient, gives somewhat better control of the anesthetic agent, as well as stimulates some cough reflex at the time the

anesthetic is injected. Again it should be stressed that one of the important phases of bronchoscopy is to stimulate the cough reflex, and whenever possible this should be done. Doing the procedure slowly is of great aid, for any secretions which are freed by the vasoconstrictor can be removed.

SUMMARY

In patients afflicted with chronic respiratory illnesses characterized by obstruction of smaller airways, acute bronchitis and bronchiolitis can lead to severe ventilatory insufficiency due to obstructing secretions.

The type of lungs in which this respiratory emergency occurs is characterized by lobular obstruction, lobular atelectasis and infection, fibrosis, compensatory emphysema of neighboring lobules, distortion of airways (kinking), cyst formation, compression by cysts of contiguous lobules, increased pulmonary vascular resistance—all producing pulmonary insufficiency. With the addition of acute infection or irritation, exudation and hypersecretion lead to lobular drowning, thickening of alveolar-capillary membrane and increased pulmonary vascular resistance. An acute respiratory emergency ensues.

The clinical syndrome of acute obstructing bronchiolitis is characterized by severely diminished ventilation, poor tussive force, very limited wheezing due to grossly restricted airflow, cardiac arrhythmias, cor pulmonale, stupor, coma, and leukocytosis.

For successful treatment, removal of secretions, anti-inflammatory agents including both antibiotics and adrenal corticosteroid hormones, and maintenance of alveolar ventilation must be employed. Of critical importance in therapy is the careful bronchoscopic aspiration of secretions, performed with minimal anesthesia.

Mason Clinic

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XCII

THE CORRELATION OF BRONCHOSCOPIC AND BRONCHOGRAPHIC FINDINGS IN THE MIDDLE LOBE SYNDROME

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Although the statement has been made that a definite diagnosis of the middle lobe syndrome can be made only by surgery and not on the basis of clinical, bronchoscopic and radiologic findings,[7] I believe this to be incorrect. The purpose of this paper is to show that by the use of bronchoscopy and bronchography, this syndrome can be diagnosed with certainty.

In 1948 Graham et al[4] reported on chronic obstructive pneumonitis of the right middle lobe, which since then has been given the name of the middle lobe syndrome. There have been many articles on this subject since then and there seems to be no doubt in the opinion of the majority, that this is a definite clinical entity. Rubin and Rubin[8] saw no need to designate this condition a syndrome because of an anatomical peculiarity. Harper[5] et al were unable to find that it was a correlated clinical and pathological entity. In this they were supported by Fretheim.[3] Kross and Rosenblatt[6] believed that this is the same clinical entity described by Eliasberg and Neuland as epituberculosis and by Prosoroff in 1929.

The condition originates primarily as a bronchostenosis of the right middle lobe bronchus as a result of the anatomical peculiarity of this bronchus. The right middle lobe bronchus originates at an acute angle from the right stem bronchus about 2 cm below the orifice of the right upper lobe bronchus. It is encircled by three or more peribronchial lymph nodes which are at the apex of the lymphatic pathways from both the upper and lower lobes as described by Brock.[10] The bronchus is 2 cm or more in length before it divides into the medial and lateral segmental bronchi. An infection originates in the lung parenchyma and there is a resulting lymphadenopathy of the nodes surrounding the middle lobe bronchus, producing

From the Veterans Administration Hospital, Tucson, Arizona.

Figure 1

compression of this easily compressible tube. If this mechanical compression is temporary, no permanent damage results. If the lymphadenopathy persists, parenchymal changes in the lung occur, due to the stenosis produced by the lymphadenopathy and by edema and even stricture of the bronchus as a result of spread of the infection through the bronchial wall from the lymphnodes. A secondary obstructive pneumonitis ensues, resulting in bronchiectasis, or, if the obstruction is permanent, in atelectasis. As Buis and Cole[1] have stated, for a portion of a lung to become atelectatic two factors must be present. The source of air must be eliminated and there must be sufficient circulation to remove the trapped air. The reversibility of the atelectasis depends on the duration of the state of airlessness, the amount of inflammation and the fibrous tissue formation. The whole

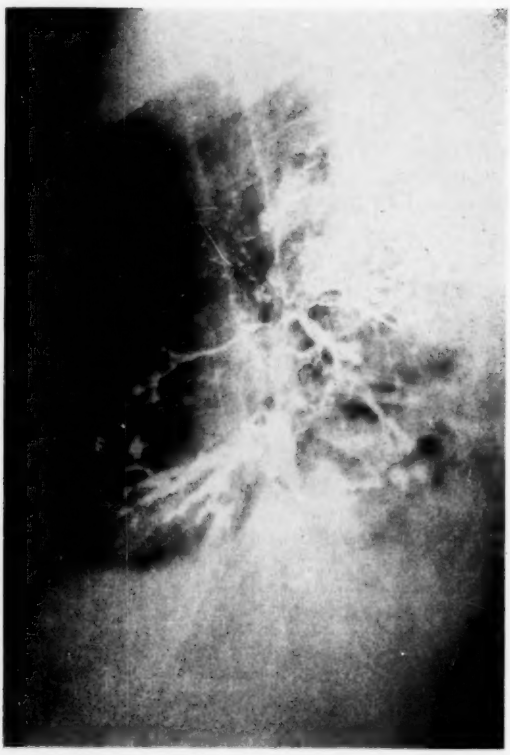

Figure 2

condition seems to be a vicious cycle as Graham et al[4] originally described it. No one factor is responsible, but the sequence of events consists of inflammatory process, lymphadenopathy, broncho-compression, bronchostenosis, atelectasis and perpetuation of the lymphadenitis by the pneumonitis produced by the obstruction.

The etiological agent is thought by most to be viral or bacterial, though Kross and Rosenblatt[6] believe tuberculosis is usually the factor. Cohen[2] reported eight cases dues to bronchial perforation by tuberculous lymph nodes and Fretheim[3] found pervious tuberculous infection in 7 of 19 cases of middle lobe bronchostenosis. Valle and Cloutier[9] reported a case of right middle lobe atelectasis due to bronchial com-

Figure 3

pression by enlarged lymph nodes produced by esophagitis following the swallowing of a part of the broken denture.

The cases reported in the literature have occurred in any age group from childhood to old age and in an equal sex ratio. The condition may be asymptomatic and found initially on routine x-ray examination, but usually it is accompanied by chronic cough, easy fatigability and hemoptysis. Radiologically a shadow is noted especially in right lateral chest films in the area of the right middle lobe.

A definite diagnosis of middle lobe syndrome can be made by bronchoscopy and bronchography. Bronchoscopy will reveal varying degrees of inflammatory stenosis of the middle lobe bronchus. The orifice may be slightly injected, compressed to complete obstruction and contain secretion which may be thick and blood-tinged.

Figure 4

Figure 5

TABLE I

CASE	SEX	AGE	BRONCHOSCOPY	BRONCHOGRAPHY	PATHOLOGICAL REPORT
1.	M	36	Orifice injected	Lobe did not fill	Lobe shrunken and atelectatic
2.	M	39	Orifice injected and secretion present	Bronchiectasis	Atelectasis and bronchiectasis
3.	M	33	Secretion	Bronchiectasis	Atelectasis. Bronchus surrounded by lymph nodes
4.	M	25	None	Bronchiectasis	Atelectasis and bronchiectasis
5.	M	38	None	Bronchiectasis	Bronchiectasis. Lymph nodes enlarged
6.	M	32	Orifice compressed. Secretion	Lobe did not fill	Bronchiectasis and large mass of lymph nodes compressing bronchus
7.	M	34	Orifice injected and secretion present	Bronchiectasis	Atelectasis and bronchiectasis
8.	M	66	Orifice injected and secretion present	None. Atelectasis on x-ray	No surgery
9.	M	41	Thick, blood-tinged secretion	None. Consolidation and cavity on x-ray	Abscess
10.	M	32	Creamy secretion	Lobe did not fill	Bronchiectasis
11.	F	28	None	Bronchiectasis	Atelectasis and bronchiectasis

Bronchography may show narrowing or complete obstruction of the bronchus by its failure to fill. If the obstruction has been relieved, the distal bronchi may show close grouping of the bronchi due to atelectasis.

The 11 cases which have been observed at this hospital (Table I) illustrate the various combinations of findings which may be seen on bronchoscopy and bronchography. Cases 1, 6 and 10 showed failure of the right middle lobe bronchus to fill at the time of bronchography (Figs. 1, 2, 3) but at bronchoscopy only Case 6 revealed compression of the bronchus, Case 1 showing injection of the orifice and Case 10 the presence of creamy secretion. Cases 2, 3 and 7 showed evidence of

bronchiectasis on x-ray examination (Figs. 4, 5) and at the time of bronchoscopy, all three showed the middle lobe orifice to be injected and containing thick secretion. Cases 8 and 9 showed injection of the orifice and the presence of secretion on bronchoscopy, but bronchography was not performed. Cases 4 and 5 demonstrated bronchiectasis on bronchography, but were not bronchoscoped. Ten of these cases underwent surgery and all were found to have a destructive process in the right middle lobe. In three of the cases a large mass of lymph nodes compressing the right middle lobe bronchus was found.

SUMMARY

The etiology, anatomy and pathology of the middle lobe syndrome have been reviewed. It has been demonstrated that by means of bronchoscopy and bronchography a definite diagnosis of this condition can be made prior to surgery.

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XCIII

COMFORTABLE BRONCHOSCOPIES USING THE SITTING POSITION

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A departure from the conventional supine position for elective bronchoscopies seems helpful in making them more enjoyable to the patient. The descriptions of a bronchoscopy have always made patients somewhat apprehensive, especially if related by fellow patients or friends who some times take malicious delight in exaggerating the details of having a large tube shoved down one's throat.

The climax of the apprehension seems to come when the patient is moved to the operating table, requested to lie down and be strapped in place. The more apprehensive patients are particularly prone to rebel, request a general anesthetic or even express a desire to postpone the procedure at this stage.

A general anesthetic for bronchoscopy has several disadvantages. Such an anesthetic for the introduction of the bronchoscope must be deep enough to provide sufficient relaxation so that the patient may open his mouth wide. A light anesthesia provides temporary amnesia, but not relaxation and the chipped teeth and sore throat following it are lasting mementos of the procedure. An anesthesia of the depth required for relaxation interferes with the co-operation of the patient in coughing at the proper time to assist in the evacuation of secretions from his lung abscess, bronchiectatic cavities or atelectatic lobes, thereby defeating the purpose of the bronchoscopy. One hesitates to irrigate the bronchi with the customary 30 to 50 cubic centimeters of saline for tumor cell examination when the patient is completely anesthetized and may not expel the fluid readily. A general anesthetic requires and prolongs hospitalization for 24 to 48 hours.

Avertin® was used by the author for all bronchoscopies for several years according to the custom of the institution in which he worked at that time. It provided temporary amnesia, but relatively little relaxation, and there was great difficulty in prying open the patient's mouth. Pentothal® provides quick relaxation but also pro-

duces laryngeal spasm and apnea, which has required artificial respiration on a number of occasions. Psychotherapy and reassurance with a mixture of vocal and local anesthetic helps a great deal in all except the patients who need it the most, such as alcoholics and retired pugilists.

The most difficult patients to persuade to recline are the orthopnoeic ones; and indeed no attempt should be made to force these patients down and further impair their limited respiratory reserve. This applies particularly to the decompensated cardiac patient, about to lapse into acute pulmonary edema with frothy secretions pouring out of the bronchoscope, if forced to assume the recumbent position. A bronchoscopy was considered to be contraindicated in such patients a few years ago, but these are the very ones who need a bronchoscopy the most if their decompensation is associated with a bronchial obstruction. Other patients who have difficulty lying down are those with bilateral pneumonia, massive atelectasis, emphysema, or a combination of these diseases. Contrary to some present theories that emphysema patients should be taught to lie down in a Trendelenberg position, it has been the experience of the author that such patients either refuse to assume such a position, or at best tolerate it for only very brief periods.

The sitting position was first used by the author for bronchoscopies on orthopnoeic patients of necessity, and at their request. No claim of originality is being made because it is well known that the sitting position has been used by some bronchoscopists for many years. Acutely ill patients and special circumstances have required most bronchoscopists to adapt themselves to peculiar positions of patients in bed. Possibly the simplest of such positions for bronchoscopy is one with the upper half of the patient's bed elevated to a semi-Fowler's position, permitting the operator to work over the head of the bed.

Brronchoscoping these orthopnoeic patients in a wheel chair proved to be such a simple procedure that its use was gradually extended during the past two years to all bronchoscopies and esophagoscopies with the exception of children.

Several advantages of the sitting position immediately become apparent to the surgeon and hospital staff. Less premedication is required since the patient does not object to being more alert during the procedure. This makes out-patient treatment more feasible, eliminating the necessity for all of the tedious admission and discharge routines now required by hospital record rooms, including records

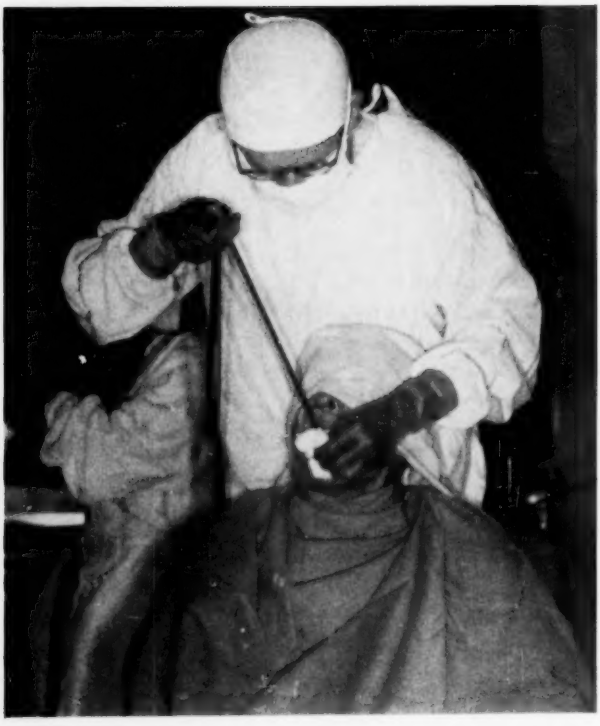

Fig. 1.—Insertion of bronchoscope with patient upright in wheelchair.

of histories, physical examinations and progress notes. Time and effort is saved by eliminating the necessity for transferring the patient on and off the operating table since he remains in the same wheel chair throughout his transportation, anesthetization and bronchoscopy. No burly orderly is required to hold down the patient's shoulders on the operating table. The present era of rapidly changing hospital personnel, with inadequate and untrained assistance, makes all of these labor saving features seem more important than previously.

Use of the sitting position also has several advantages for the patient. The economic factor of being able to use out-patient facilities with less premedication reduces the cost of the procedure by about 25 per cent by eliminating a day's room rent and all of the routine admission laboratory examinations. Elimination of transfers reduces

the operating room time and consequently the operating room expense. Patients complain of less psychic trauma associated with being strapped to the operating table. They have less sore throat and less postoperative tenderness of the abdominal musculature, since it is easier to cough in a sitting position than in a supine position. These latter claims have been made by patients who have been bronchoscoped at various times in both positions.

A few limitations exist for use of the sitting position. Comatose patients or patients under a general anesthetic are obviously unsuitable. The sitting position is not practical for babies and nervous children who require considerable restraint. It should not be used for direct laryngoscopies except the most cursory type of examination associated with passage of the bronchoscope to determine mobility of the vocal cords.

A few fundamental principles and pieces of equipment are required to make a bronchoscopy successful in the sitting position. First, a sturdy modern low wheelchair is needed with a metal frame and low back. The older high-backed wooden wheelchairs are unsatisfactory. The chair is held in place by its brakes or by sand bags. An adequate seat belt is a very important part of the equipment, for without it the patient tends to straighten his body, lean back too far, and slide down in the chair. A wide leather belt passed around the patient's waist and under the seat on one side and behind the post supporting the chair back on the other side keeps the patient's hips back and prevents him from sliding down in the chair. It is unsatisfactory to strap the patient to either the seat or to the back of the chair alone. He must be strapped to both at once.

A headholder, if available, stands at the patient's left holding a bite block in the left side of the patient's mouth with the left hand and supporting the back of the patient's head with his right hand.

The operator stands behind the patient on a low footstool for the insertion of the 'scope, following which he steps down on the floor and pushes away the stool. Additional support can be given the patient's head with the operator's hip or abdomen if necessary. The scrub nurse stands at the patient's right side.

CONCLUSIONS

1. The sitting position is recommended for all bronchoscopies except those on infants, children, or comatose patients.

2. Lighter premedication is required for the sitting position permitting a larger percentage of bronchoscopies on out-patients with reduced expense for the patient and effort for the surgeon.

3. An upright position is absolutely essential for orthopnoeic patients and less traumatic and frightening for other patients.

4. Remaining in the same wheelchair throughout the transportation, local anesthetization and operation saves time and effort for the staff.

5. Fewer trained assistants are required for the use of the sitting than the supine position.

6. Adequate fixation of the patient's hips by a tight seat belt greatly facilitates the procedure.

MAYER BLDG.

XCIV

ADDITIONAL EXPERIENCES IN BRONCHOTOMY FOR BRONCHIAL ADENOMA

ALFRED GOLDMAN, M.D.

BEVERLY HILLS, CAL.

Bronchial adenoma comprises a group of histologically different tumors usually located in a stem or lobar bronchi, of epithelial origin, slow growing and rarely metastasizing. The malignant nature of these tumors has been under considerable scrutiny and controversy.[6,7]

To over-simplify the present status, one could say that all bronchial adenomata are malignant and therefore their treatment should be consistent with the treatment of malignant tumors elsewhere in the body, namely, resection of the entire organ or its anatomical unit together with the draining lymphatics. On the other hand, one can take the point of view that the malignancy or benignancy varies according to histological types and their gross and microscopic characteristics so that we have in this group of tumors some that respond well to local excisional types of therapy such as bronchotomy and others that do not. We believe that those tumors amenable to local excision can be differentiated from their more invasive and malignant species of adenomata. Graham and Womack[2] were among the first to indicate the malignant properties of bronchial adenomata, and they implied that pneumonectomy was the most logical procedure. Brunn,[8] on the other hand, felt that there were different kinds of tumors in this group, and it is the purpose of this paper to show that there are types of bronchial adenomata amenable to local excisional therapy and especially via the transpleural bronchotomy technique.[9-12]

Because bronchial adenomata are relatively rare and because location of the irreversible suppuration of the lung may make it unwise to even attempt bronchotomy, the number subjected by us to bronchotomy has been only seven, and of these only five, or approximately 7%, have actually been resected. From our experience, then,

From the Thoracic Surgical Services, City of Hope Medical Center, Duarte, and Cedars of Lebanon Hospital, Los Angeles.

the criteria for transpleural bronchotomy markedly limit the number of patients in whom this operation is amenable. These criteria at present may be changed as a larger number and further follow-up occur; nevertheless we feel that we can set down the following indications for operation:

1. Histological variety conforming to carcinoid or serous glandular types. (It is understood that in all probability there are rare benign tumors of the bronchus including lipoma,* neurofibroma and glandular cell myoblastoma which may also be amenable to this procedure.)

2. Location in an accessible bronchus, usually lobar, or stem, or the lower end of the trachea or the carina.

3. Preferably a stalk-like attachment. Sessile attachments with intramural involvement should not extend through more than five cartilaginous rings for satisfactory result.

4. Well-confined and localized tumors recurring after bronchoscopic removal.

5. Absence of malignant degeneration with metastases or widespread bronchial wall infiltration.

6. Supple bronchial wall amenable to suture without production of stenosis after local excision of the tumor.

7. Absence of irreversible pulmonary suppuration, and with the state of the distal lung such that it will not become a future hazard.

8. Absence of extensive extra-bronchial growth.

9. Absence of extension to regional lymph nodes.

10. State of pleural cavity and hilum of the lung which will lend itself to easy access of the large bronchi containing the tumor. (In one instance, we have successfully performed decortication for chronic empyema of the lung with transpleural bronchotomy. Case No. 5.)

Tumors and conditions in which transpleural bronchotomy is contraindicated:

1. Cylindroma, giant cell bronchial tumors or myosarcomas.

2. Carcinoids with lymphatic extension.

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* Fourteen months ago, we successfully performed transpleural bronchotomy and excised a lipoma of the segmental bronchus of the left upper lobe.

3. Extensive extrabronchial growth especially with distal putrid abscess of the lung.

4. Carcinoids involving two lobar bronchi and the segmental orifices.

5. Adherence to large pulmonary vessels too intimate for safe dissection.

6. Old carcinoids with distal carnified lung and fibrotic pleura or empyema.

7. Aged and debilitated patients in whom palliative bronchoscopic opening of the bronchus can be readily accomplished.

Bronchoscopic removal will always be valuable for diagnosis and re-establishment of bronchial drainage in obstructing adenomata.[13-15] Bronchoscopic procedures in several sittings may be necessary before establishing the presence of a recurrence, obtaining adequate bronchial drainage or even adequate biopsies of the tumors; however, it has been shown repeatedly that it is extremely unlikely that all of the tumor can be removed via the bronchoscope since so many tumors invade the bronchial wall beneath the mucosa. On the other hand, in the carcinoid variety it may take many years before manifestations of growth of the intramural portion are evident (Case 1).

It is hoped that in the future the bronchoscopist will make the diagnosis much earlier than he has in the past,[16] thus making it quite likely that local excision via transpleural bronchotomy may be applied to smaller, less invasive tumors with less damage to the distal lung and therefore more preservation of pulmonary function. If these tumors can be discovered in late childhood or the teenage group, one can prevent the chronic morbidity associated with decades of pulmonary suppuration which have occurred in the past. Bronchoscopic examination is the only way to make the diagnosis early in these young people.[17] A higher percentage of patients should be amenable to transpleural bronchotomy when the tumor is discovered in this age group (Case 3).

Technique of transpleural bronchotomy (TPB) was pioneered by Eloesser[10] in 1940. Our published case reports in 1952 show detailed techniques which we have used.[12] These include left and right side approaches, anterolateral and posterior approaches to the pleural cavity and the large bronchi. We have now performed:

1. Incision through the bronchial wall, usually the cartilaginous portion, with removal of the tumor and cauterization of the base of the pedicle of the tumor as the simplest procedure. Case. No. 3.

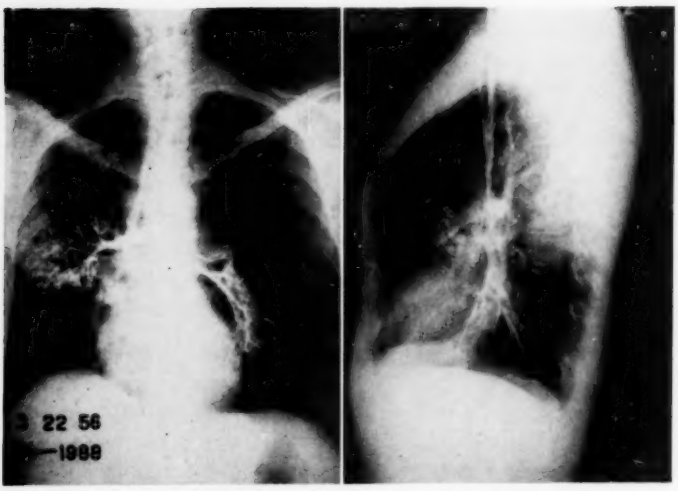

Fig. 1.—Case 2, M.Z. 3-22-56 PA and lateral bronchograms preoperative showing bronchial obstruction of right stem bronchus at level of RUL bronchus. Note the absence of filling of all the right lung below the RUL opening and also the puddling around the tumor which projects into the right stem bronchus to the level of the carina.

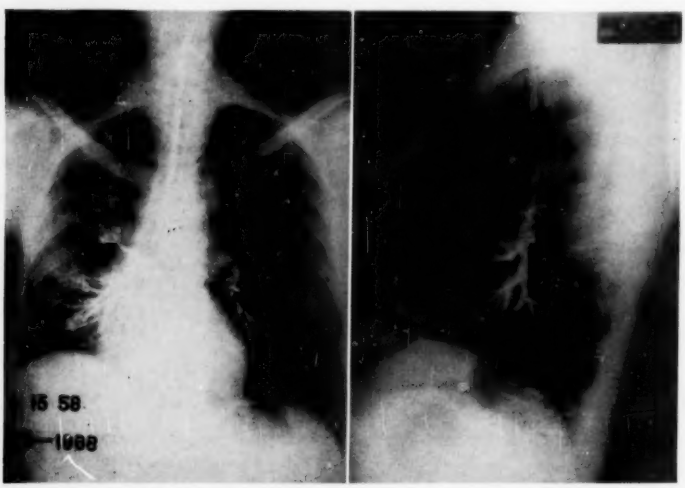

Fig. 2.—M.Z. 4-15-58 PA and right lateral bronchograms two years and six weeks after TPB with sleeve resection of intermediate bronchus. Note the filling now of RML and RLL which did not fill before (see Fig. 1) and also the absence of significant bronchiectasis.

Fig. 3.—Case 2, M.Z. Gross specimen of muco-epidermoid carcinoma (or possibly serous glandular adenoma). Bronchus has been opened lengthwise. Note the sessile attachment and extrabronchial tumor.

2. Excision of a portion of the wall including two or more bronchial rings with the tumor. Case No. 4.

3. Sleeve excision of segment of stem bronchus with reimplantation in the trachea. Case No. 2.

4. Lobectomy, combined with excision of recurrent tumor in a stem bronchus with conservation of the upper lobe on the left. Case No. 1.

5. Concomitant decortication with right stem bronchotomy and resection of several rings of the right stem bronchus containing endobronchial and intramural obstructing adenoma. Case No. 5.

In addition to these, unsuccessful attempts were made in three additional patients in whom the transpleural bronchotomy could not be done because of the nature and location of the adenoma. In all of these, one or more of the contraindications were present.

All five of these patients have been personally examined within the past few months with the exception of Case No. 1 which has been followed by Dr. Clayton Lyon, of San Francisco, who has furnished me with a recent report. These patients are now alive without clinical evidence of tumor, as follows:

Case No. 1, A. B., TBP. 1946, no evidence of recurrence 12 years postoperatively.

Case No. 2, M. Z., TPB. March. 1956, sleeve bronchial resection, diagnosis muco-epidermoid carcinoma (similar to Case No. 3), alive and well 2 years and 2 months postoperatively.

Case No. 3, D. P., TPB. 1949, living and well 9 years postoperatively.

Case No. 4, S. S., TPB. 1949, living and well 8½ years postoperatively.

Case No. 5, S. C., TPB, with decortication for chronic empyema, 1956, no evidence of recurrence, 2 years postoperatively.

These five cases, in which total excision via transpleural bronchotomy was performed, show no evidence of recurrence, the longest times being over 9 years and 12 years. In cases No. 1, 3 and 4, all three of which are approaching or are beyond the 10 year period, careful follow-up has shown no evidence of recurrence. It seems that there is little likelihood that it will occur. (These represent cases No. 1, 3 and 4 which were previously published in 1952,[12] and 1947 [see case No. 10][9].) The follow-up studies on these three cases definitely show that TPB gives lasting results, tantamount to 10 year cures, and is thus an acceptable procedure for serous glandular adenoma and carcinoid adenoma. These three cases also show that pulmonary function is preserved by TPB as opposed to pulmonary resection such as pneumonectomy. Although the earliest three cases, Nos. 1, 3 and 4, had been previously published with follow-up until 1952, Cases Nos. 2 and 5 have never been reported; therefore they are summarized here.

Case 2. (City of Hope Medical Center Hospital No. 55-1988). This 42 year old white male had an onset of symptoms in the summer of 1952 and hemoptysis of approximately 2 tablespoonfuls of red dark blood. Although he was examined regularly by physicians in the Public Health Department, nothing was found until April, 1954, when the first bronchoscopy was done and the bronchial aspirations were positive for acid-fast bacilli. On the basis of this single finding and one positive sputum test he was transferred in 1955 to this hospital's Tuberculosis Division, and was placed on the usual triple treatment. The course of the disease was complicated by regional ileitis and in January, 1956, a resection of 150 cm of small and 30 cm of large bowel was done. During his convalescence he again had recurrent hemoptysis in February, 1956. Bronchoscopy

was performed March 16, 1956, and this showed a vascular tumor in the medial wall and obstructing the intermediate right bronchus. No diagnosis was rendered on the first biopsy. A bronchogram showed blockage of the right middle and lower lobe. On March 21, 1956, transpleural bronchotomy was performed with resection of the intermediate bronchus and a portion of the right upper lobe bronchus, and with reimplantation of the right lower lobe and incised right upper lobe into the trachea.

The specimen consisted of a well-circumscribed, apparently encapsulated tumor measuring 3 x 2.2 x 2 cm, the surface of which was slightly bosselated. Adherent to the tumor was fibrous and fibro-adipose tissue, including on the under surface a small lymph node, 1 cm in greatest diameter, and a fairly large nerve crossing the specimen on the undersurface. The tumor was attached to the bronchial wall by a short pedicle 1 cm in length, although it was adherent to the bronchial wall over an area of 3 cm. A sub-pleural calcified nodule was also resected at the time of the operation. A specific diagnosis could not be made of this. It probably represented healed tuberculosis. The pathologist's report (Dr. Fred Preuss) follows:

> The tumor presents, microscopically, a varied picture. There are large areas in which the tumor appears fasciculated; nests and strands of densely packed cells with abundant fairly clear and slightly granular acidophilic cytoplasm and moderately-sized vesicular nuclei containing frequent small nucleoli are separated by thin strands of connective tissue. Mitotic figures are moderately frequent. In such areas the tumor resembles a clear celled carcinoma. In other areas, however, it forms glandular structures, the lumina of which are filled with a homogeneous mucoid material. There are intervening areas of calcification and degeneration. The latter contain numerous cholesterol clefts. The tumor is in very close proximity to the bronchial cartilages and invades the latter rather extensively. There are other areas where the invasion of the tumor capsule is clearly evident and vascular invasion is strongly suggestive. Periodic acid Schiff (PAS) stains showed red staining indicative of mucin within the glandular structures. The lymph node was not involved.

Dr. Preuss's diagnosis was "mucus forming adenocarcinoma with probable origin in the mucous bronchial glands." Dr. George Amromin's diagnosis was "muco-epidermoid carcinoma." The opinion of the pathologists was that the tumor represented borderline malignancy.

The postoperative course was complicated by bronchial obstruction which responded well to tracheal aspirations and the right lung became well-aerated. The patient was able to return to work within a few months after the TPB and two years later on April 14, 1958, was readmitted for further study. Although he was still having some

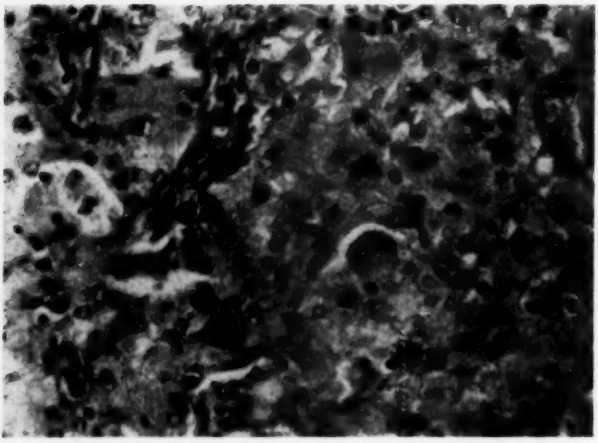

Fig. 4.—Photomicrograph, Case 2, M.Z., showing sheets of cells of epidermoid character.

Fig. 5.—Photomicrograph of surgical specimen, Case 2, M.Z., showing large spaces filled with mucus; periodic acid Schiff stain.

diarrhea, he had been relatively free from pulmonary symptoms since his discharge following the TPB. Following discharge on June 5, 1956, he worked regularly as a truck driver. At bronchoscopy April 15, 1958, some thickening of the mucosa was seen about the orifice of the middle lobe and a moderate amount of secretions of the mucoid type were sucked out of the right upper lobe and the remains of the right stem bronchus. The bronchial orifices were widely patent. A biopsy specimen was taken from the region of the right middle lobe which showed no evidence of tumor. Cytological examination of the aspirated secretions showed scattered atypical epithelial cells not diagnostic of carcinoma, which were considered as possibly originating from zones of bronchiectasis. Atypical squamous cells which were also seen were thought possibly to arise from areas of squamous metaplasia.

During this admission a bronchography was also performed which confirmed the patency of the right lobar orifices without disclosing any marked bronchial dilatations.

SUMMARY OF CASE 2 (M.Z.). This is an unusual variant of bronchial adenoma with a past history of asthma followed by hemoptysis and the duration of symptoms at least five years before the TPB. In the two years and two months since local excision with sleeve resection of the right intermediate bronchus there has been no sign of recurrence in spite of the stigma of malignancy suggested in the pathological reports.

CASE 5 (S.C., City of Hope Medical Center No. 56-1423). Onset with pneumonia, pleuritic right chest pain, hemoptysis and wheezing that occurred in a 53 year old white female two years before admission. Bronchoscopy performed elsewhere shortly before admission disclosed a tumor obstructing the right stem bronchus just below the carina. Pleural fluid was aspirated from the right chest and a second bronchoscopy on November 13, 1956, showed the carina to be sharp and deflected to the right side. The left main stem bronchus was normal. Within the right stem bronchus, approximately ½ cm below the carina an obstructing cauliflower-like mass which completely occluded the lumen was encountered. The tumor extended above the level of the right upper lobe orifice and partially obstructed it. Specimens were taken which showed small gland-like structures containing cells somewhat pleomorphic, with dark-staining nuclei. Cytological study of secretions and smears showed no evidence of malignant cells nor of unquestionably neoplastic cells. Diagnosis was atypical bronchial mucosa and no evidence of malignancy.

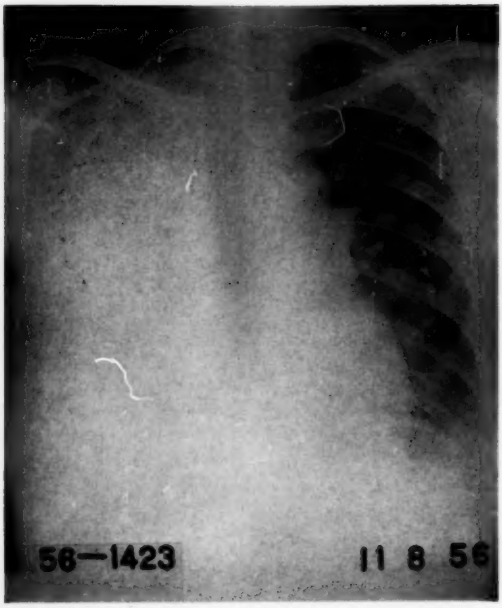

Fig. 6.—Case 5, S.C. Preoperative film 11-8-56. Chest: There is complete obliteration of the right thorax. There is slight shifting of the mediastinum to the left. The left lung field is clear. The changes on the right are due to a massive pleural effusion. The condition of the underlying parenchyma cannot be evaluated. Skeletal survey: No evidence of metastatic disease. There is noted calcification in the abdominal aorta. In addition, there is a calcified lymph node in the right lower quadrant.

X-ray films of the chest disclosed complete opacity due to purulent fluid and after aspirating 1100 cc the lung could be seen to be held captive against the right mediastinum. On December 4, 1956, after suitable preparation with antibiotics, a right upper lobectomy and decortication of the chronic empyema peel was done, together with bronchotomy of the right stem bronchus and local excision of the blackish necrotic tumor it contained. The right upper lobe was removed because the tumor invaded a portion of the right upper lobe bronchus and, in spite of thorough decortication, the right upper lobe did not aerate well. Even the right lower and middle lobes did not fully re-expand after resection of the tumor and aspiration of large quantities of mucoid material from their bronchi. Decision not to resect these lobes was made on the basis that if they should

expand later they would at least be space-filling, if not actually developing some function. The specimen of the bronchial tumor consisted of three irregular pieces of tissue; one of them was 5 mm in its greatest dimension and was pink-grey. The other two pieces measured 2 x 1 x 1 cm and 1½ x 1 x 0.5 cm respectively. The pleura and the lung were also examined. Microscopically, the tumor presented relatively neoplastic cells infiltrating in cords and occasionally forming pseudo-alveolar structures. In many areas the tumor cells were arranged over vascularized fibrous connective tissue stalks or appeared to surround small blood vessels. The tumor cells, for the most part, were tall, cuboidal or columnar, and in many areas were arranged in rows. The endobronchial portion showed extensive superficial necrosis, ulceration and hemorrhage. Smooth muscle at the base of the endobronchial portion was infiltrated with tumor cells. Mitoses were relatively rare and a thick fibrous connective capsule or pseudocapsule demarcating the tumor from the surrounding lung was seen. There was definite tumor in the right upper lobe bronchus which was resected. The tumor tended to grow under the bronchial mucosa.

Dr. George Amromin's diagnosis was "papilliferous undifferentiated carcinoma with features of bronchial adenoma, superficially necrotic and ulcerated."

The postoperative course was complicated by a recurrence of empyema which required an Eloesser flap drainage. This has continued to drain slightly until the present time. The drainage was performed January 29, 1957, and at this time the pleural cavity was re-explored and biopsies were done. No evidence of neoplasm was found at biopsy nor was there any evidence of grossly visible or palpable tumor. The residual right lung was partially re-expanded and was adherent to the diaphragm and posterior and anterior chest walls. Although a bronchopleural fistula had been diagnosed at the time of the exploration of the pleural cavity, none could be found.

The empyema cavity held less than 500 cc and cultures showed staphylococcus aureus. Radiologically there has been a decrease in the empyema, with slight increase in the size of the underlying lung. The patient was last seen on April 28, 1958, at which time her general condition was good, the Eloesser flap had narrowed down to a sinus tract and required finger dilatation to maintain patency.

X-ray films of the chest were made at this time (Fig. 6).

SUMMARY

This case is significant in that it is the only one in which we performed a TPB in the face of a chronic empyema. Although the end result has been satisfactory so far (2 years and 2 months), the remaining lower and middle lobes which were conserved have not become completely aerated. Neither have they caused any attacks of fever or pneumonitis, which might have been expected. Again, the histological diagnosis is clouded by features of malignancy and we will continue to observe this patient for evidences of recurrence.

416 N. Bedford Drive

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ERRATUM

In the article entitled "Collagen Diseases of the Upper Respiratory Tract," by Prof. Michele Arslan, June issue, page 287, line 24, for "Muscle biopsy has always given positive results." read "Muscle biopsy has always given negative results."

CHEVALIER JACKSON, M.D.

1865 - 1958

Dr. Chevalier Jackson, whose name has long been synonymous with endoscopy in all its phases and who played a leading role in the teaching of this specialty, died in Philadelphia on August 16, 1958.

He was born November 4, 1865, at Pittsburgh, Pennsylvania, and graduated in medicine from Jefferson Medical College in 1886. Early in his practice he began specializing in laryngology in Pittsburgh, Pennsylvania, where he later became Professor of Laryngology at the University. It was in Pittsburgh that his name gradually became linked with the young and growing specialty of endoscopy, in which he was destined to play such an important role.

In 1916 he returned to his alma mater, Jefferson Medical College, as Professor of Laryngology, and a few years later was given the newly created Chair of Bronchoscopy and Esophagoscopy at the University of Pennsylvania. In 1924 his title at Jefferson was changed to Professor of Bronchoscopy and Esophagoscopy and about this time he was given a lectureship in Temple University, where later he became professor.

He devoted his life to developing and systematizing instruments and operating procedures in endoscopy, and to the teaching of his methods in this country and abroad. In recognition of his contributions he was made a Chevalier of the French Legion of Honor and of the Belgian Order of Leopold in 1927, after which there was a long succession of honors, medals and awards from numerous foreign countries and from medical societies all over the United States.

At various times in the course of his career he became President of the American Laryngological Association, the American Therapeutic Society, the Woman's Medical College of Pennsylvania, the American Bronchological Association and the Pan-American Medical Association. He was one of the founders of the American College of Surgeons and the recipient of honorary degrees from Jefferson Medical College, Ursinus College, Pennsylvania Military College and the Woman's Medical College of Pennsylvania. In 1926 he received the DeRoaldes Award of the American Laryngological Association, in 1933 the Gold Medal of the Radiological Society of North America,

CHEVALIER JACKSON

and in 1940 the Distinguished Service Medal of the American Medical Association.

He was tireless in his propaganda for the enforcement of proper labelling of caustic poisons and was Chairman of the Committee on Lye Legislation of the American Medical Association. In 1927 he was instrumental in obtaining the passage of the Federal Caustic Poison Law.

He was a severe taskmaster to himself and to his students and the perfection of detail in all his instruments, methods and teachings was his outstanding characteristic. He was adept at the blackboard and drew many of the pictures which illustrate his works.

He was never a convivial man and even in his contacts with colleagues and students he was apt to be aloof while ever maintaining a meticulous courtesy. Aside from the unsparing drive which he gave to all his work, he led a simple life and retained his mental faculties until his death at 93.

He was one of the key medical figures of his era.

Abstracts of Current Articles

EAR

Cholesteatoma of the Temporal Bone

Chiat, Harold, and *Kittredge, Richard D.*: Radiol. 71:4:559-562 (Oct.) 1958.

In a series of 74 mastoidectomies seen during a ten year period at the New York Hospital 28 cholesteatomas were found at operation. Preoperative roentgen diagnosis was possible in 13. Practical problems arising in the roentgen diagnosis and value of tomographic studies are discussed in relation to a possible increase in number of cases correctly diagnosed. Figures include a roentgenogram, two tomograms and a drawing. Six references are cited.

JORSTAD

The "Transplant Cholesteatoma" (A Late Complication After Tympanoplasty)

Beikert, P.: Zschr. Laryng. 37:567-572, 1958.

The author, who is associated with Dr. Zoellner in Freiburg i.Br./Germany, reports upon a complication after tympanoplasty: the occurrence of cholesteatoma-like growths within the skin transplant. These cholesteatomata do not represent recurrences, although clinically the two forms are often difficult to differentiate. At the Freiburg clinic, the transplant cholesteatoma has been seen so far in six cases among a total of 400 tympanoplasties. The time of development on the average was two years.

When the situation is recognized early, there is nothing but an epithelial cyst within the otherwise intact transplant and the process can be arrested simply by opening and cleaning of the cyst. Thereby the drum head can be preserved.

In several cases, in which the epithelial growth had apparently first developed toward the tympanic side, the old transplant had to be removed surgically. This made it possible to study these specimens histologically. The presence of normal skin appendices (hair follicles,

sebaceous glands) was repeatedly noted in the specimens. This finding is taken as counter-evidence against the theory that the transplant is invariably first altered into granulation tissue and then secondarily covered by epithelium growing in from the vicinity.

Since the origin of these cholesteatomata was thought to be in a) the special location of the transplant at the depth of the external canal and b) in the presence of hair follicles and glands, it was logical to attempt to find skin areas which might be free of such appendices. The author maintains that such areas do not exist. In general, the skin on the inside of the upper arm is best in this respect, although it is seldom entirely free of skin appendices. Therefore, it is advisable in each individual case to search carefully under the microscope for an optimally suited piece of skin in this area before taking the transplant.

Routine observation of all cases of tympanoplasty with special consideration to the possibility of "transplant cholesteatoma" is needed for many years after the original operation.

TONNDORF

Transmission of Sound in the Middle Ear as Seen by a Clinician

zum Gottesberge, A. Meyer: Zschr. Laryng. 37:355-367, 1958.

The renewed interest of otologists in middle-ear physiology is due to the recent progress in surgical procedures such as fenestration, stapes mobilization, and tympanoplasty. The present account by a clinician, although offering nothing strikingly new, sums up our present-day knowledge in a straightforward manner. Throughout, the author relies very much upon experimental findings, mainly those of von Bekesy, combined with clinical observations of his own.

Discussed first is the transformer action of the middle ear which includes the mode of vibration of the ear drum pertinent to this function. Intimately associated with the latter is the manner of transmission through the round window. The point is made that the normal drum head does not actually serve as a "sound protecting" device. (The latter term, much used in the German literature, was first introduced by E. Mach. Reviewer). Normally, there is no need for sound protection because of the direct coupling of the oval window to the drum head via the ossicular chain; the latter mechanism being much more effective than that between eardrum and round window. Dis-

cussed next is the effect upon transmission of simultaneous exposure of both windows to sound. In this case it is only important that there exists a difference in effective pressure upon the two windows, but it does not matter which of the two is "leading" the other.

In discussing the problem of bone conduction, the peculiar phenomenon known as the "Carhart notch" is analyzed, i.e., the improvement of bone conduction after fenestration, mainly in the region of 2000 cps. Ranke in Germany has explained the phenomenon as resulting from introducing an asymmetry in mass between both perilymphatic scala: the effective mass of scala vestibuli (i.e., its volume) is increased by including part of the horizontal canal up to the point of the fenestra nov-ovalis. This results in improvement of the so-called inertia type of bone conduction. The second type of bone conduction (i.e., "compression" of the labyrinthine spaces due to vibrations of the osseous capsule) must be inversely affected by producing an "escape valve," viz., the newly created window. This becomes apparent when the new window is made in the region of the oval window so that the two perilymphatic scalae remain symmetrical. In that case, inertial bone conduction is not improved. Five clinical cases (out of a total of six in which this method was used) are cited in proving this point.

Finally, the author takes up an old argument. The statement has been made that at frequencies higher than 2400 cps all transmission ought to be via bone conduction because of Bekesy's findings that the middle ear transformer becomes less effective at about this frequency. Against this, the author cites the fact that in cases of middle-ear impairment the hearing loss is practically uniform for all frequencies which would not be the case if high frequencies were conducted by bone, and not via the middle ear. Furthermore, the observation that bone conduction above 2000 cps is not improved by occlusion of the external ear canal is explained by the fact that the ear canal ceases to emit sound above this frequency (which would otherwise contribute to bone conduction in the sense of Bekesy's findings). As to Bekesy's actual measurements, it must be pointed out that at 3000 cps the transformer ratio is still 6:1. (To this the reviewer might add 1) the ratio at 3000 cps for the combined external and middle ear is 20:1, according to Bekesy; 2) Bekesy might have been misunderstood in this respect. He has only observed that "at frequencies higher than 2400 cps the drum vibrates in segments," a fact which makes actual transmission very complex. It is recalled that microphone membranes show the same breakup in segments.)

TONNDORF

MISCELLANEOUS

Cobalt-60 Beam Therapy in Carcinoma of the Esophagus

Lott, J. S., and *Smith, Ivan H.*: Radiol. 71:3:321-326 (Sept.) 1958.

Between January 1952 and December 1956, 68 cases of carcinoma of the esophagus were seen and of these 31 were treated radically for cure. On radiographic evidence 20 of these cases had lesions 5.0 centimeters or more in length. Four cases were treated by circumaxial rotation therapy, the others through multiple ports. Tables show range of tumor dose in total treatment time, the volume treated, variations in tumor dose, survival time, and survivors free of diseases.

The optimal corrected tumor dose for squamous celled carcinoma calculated to be 6,000 to 6,500 r in four to four and one-half weeks. Treatment complications in the survivors have been few and minimal. Seven patients are apparently disease free for periods ranging from one to five years. Eight references are included.

JORSTAD

Intensive Cobalt-60 Teletherapy of Lung Cancer

Kutz, Eugene R.: Radiol. 71:3:327-335 (Sept.) 1958.

Longest survival group of 50 histologically proven cases of bronchiogenic carcinoma treated with 400 k.v. radiation between March 1, 1952 and March 1, 1955, was 56 months. The average survival time was 14.7 months. The majority of patients treated were those in whom definite evidence of nonresectability was revealed previous to or as the result of thoracotomy.

Radiation sickness occurred in patients treated with cobalt as frequently as in the x-ray series, but its severity seemed less. Esophagitis seemed to occur frequently. Skin reactions seldom required treatment even in the stationary portal cases and were nonexistent in the rotational therapy cases. Radiation pneumonitis appeared to be a more serious problem than it had been with x-rays.

One hundred and eighty-nine patients with lung cancer were treated with the cobalt bomb during 1955 and 1956. One hundred and eighty-two of these have been followed regularly. Tables of statistics are presented to show histologic type in this group and results

of treatment as reported by various authors. Twenty-four patients still survive at the end of two years. The results with cobalt were generally better than those obtained by radiation in lower energy groups.

The only series equal to or better was that reported by the author who treated all of his patients with two million volt x-rays. Treatment planning including tumor dosages is discussed. Isodose lines are illustrated on cross section anatomy diagrams. Twenty references are included.

JORSTAD

The Lateral Roentgenogram of the Neck

Wholey, Mark H., Bruwer, Andre J., and *Baker, Hillier L., Jr.*: Radiol. 71:3:350-356 (Sept.) 1958.

In an effort to establish certain normal measurements in evaluating the bony and soft tissue relationships of the neck 700 lateral cervical radiograms were reviewed. Six hundred of these were considered normal. They suggest that the following alterations in relationships warrant further evaluation of the patient: a) retropharyngeal space, b) retrotracheal space, c) relationship of posterior tracheal wall and spinal column, d) relationship of odontoid process, basion and anterior arch of atlas.

The normal values and variations, the areas and points of measurements are discussed. Twelve roentgenograms of the neck illustrate application of the technique in interpretation of pathologic findings. Seven references are included.

JORSTAD

Hematostasis Within the Bone by Means of Silicon

Neugebauer, J.: Medizinische, Nr 17, 723 (1958)

The author comments upon the disadvantages of the use of bone wax (its use had been first advocated by Horsley). The wax is brittle if its temperature is not carefully controlled and does not adhere very tightly to the bone. Furthermore, its use is not without danger (paraffinoma or even cancer) because of its content of carbonic acid.

The author has used silicon for some time instead of the bone wax and is very satisfied. It is very pliable, adheres even to smooth surfaces of bone very strongly, and is biologically inert. The silicon is dispensed from a sterilizable dispenser (build like a medical syringe) and is commercially available in two different degrees of viscosity.

The material is manufactured and distributed under the trade name Silicon by Braun, Melsungen, W-Germany.

TONNDORF

Funneling in the Nervous System and Its Role in Loudness and Sensation Intensity on the Skin

v. Bekesy, G.: J. Acoust. Soc. Am. 30:399-413, 1958

In the present paper Bekesy introduces a new neuro-physiological concept which he calls "funneling." Funneling is a combination of neural summation and inhibition. As a simple example: In listening to a sound source off to one side of the head only one ear seems to actually hear. Yet plugging up the other ear results in a decrease of loudness. Therefore, this is not inhibition of the seemingly inactive ear in the accepted sense since this ear contributes to the loudness sensation of the other one. The term funneling describes such action.

As many readers may be aware, Bekesy's interest during the past years has been focused upon the sensations produced by vibratory stimulation of the skin, that is, of the tactile sense. This research is carried out in an effort to study neural phenomena of a sense which is more readily accessible to experimentation than the auditory sense and which is furthermore an elder phylogenetic relative of the cochlea; the cochlea being of ectodermal origin.

The experiments described in the present paper concern the vibration loudness resulting from vibratory stimulation of the skin. The most interesting of these experiments, from the otologist's standpoint, compares the vibration loudness derived from broad stimulation of larger areas to that resulting from one or two point sources. When intensity was increased loudness from two-point sources increased faster than that from large areas although the latter was more sensitive than the former. This difference was especially pronounced for larger distances between two-point sources. Similar results were

obtained when the difference limen was compared between the two modes of stimulation with the aid of a modified Bekesy audiometer.

Bekesy calls attention to the similarity to the recruitment phenomenon in hearing. The following explanation is advanced which seems valid for the tactile as well as for the sense of hearing: In broad-area stimulation (in the skin as well as along the basilar membrane) many sensory cells, each stimulated subliminally, are summated resulting in a lowered threshold. The effect is the same as if only one centrally located cell is stimulated with sufficient strength (=funneling). (In a previous paper Bekesy had shown that when differently tuned vibrators are used along the skin, which are set to equal loudness, the frequencies of the lateral stimuli are suppressed and yet they contribute to the loudness of the central stimulator.) However, once single cells (or multiple cells spaced farther apart) start responding, their loudness increases rapidly in the vicinity of their (elevated) threshold (= recruitment). At still higher amplitudes, the difference becomes less pronounced because then there is also lateral spread among the cells which are spaced farther apart.

Bekesy was then able to alter the normal mode of skin response to the broad-area stimulator which ordinarily did not induce "recruitment" on the skin. This was achieved by heating up the skin thus putting some nerve endings out of action: sensitivity was lessened and the difference limen became smaller.

There are many more experimental details concerning this problem and other related experiments described in this article which cannot be reviewed here completely. Study of the original article is recommended.

TONNDORF

Books Received

Atlas of Esophageal Motility in Health and Disease

By six authors from the Sections of Physiology and Medicine of the Mayo Clinic. Cloth, 4to, 134 pp., illustrated. Springfield, Ill., Charles C. Thomas, 1958. Price $8.50.

The Cerebrospinal Fluid: Production, Circulation and Absorption

A collection of papers read by a score of authors at a Ciba Foundation Symposium and edited by *G.E.W. Wostenholme, O.B.E., M.B., M.A., B.Ch.* and *Cecelia M. O'Connor, B.Sc.* Cloth, 8vo, xii - 335 pp., illustrated. Boston, Little Brown & Co., 1958. Price $9.00.

Fundamentals, of special interest to otolaryngologists.

Comparative Anatomy and Physiology of the Nose and Paranasal Sinuses

By *Sir Victor Negus, Hon. D.Sc.(Manchester), M.S.(London), F.R.C.S.(England), Hon. F.R.C.S.(Edin.), Hon. F.R.C.S.(Ireland)*, Consulting Surgeon to the Ear, Nose and Throat Dept., King's College Hospital, Trustee of the Hunterian Collection. Cloth, Royal 8vo, xv - 402 pp., 178 illustrations. Edinburgh and London, E. & S. Livingstone, Ltd., 1958. Price 70s.

A fitting companion piece to the author's earlier work on the comparative anatomy of the larynx, which is now a classic. It offers a general survey of the nasal structures and functions with such ancillary matters as the uses of olfaction, olfactory discrimination, the various methods of breathing and temperatures in the respiratory tract, all in the author's concise style. Beautifully illustrated.

The Esophagus, Medical and Surgical Management

By *Edward B. Benedict, M.D., F.A.C.S.*, Assistant Clinical Professor of Surgery, Harvard Medical School, and *George L. Nardi, M.D., F.A.C.S.*, Clinical Associate in Surgery, Harvard Medical School. Cloth, Royal 8vo, 390 pp., 16 color plates and 108 illustrations. Boston, Little, Brown & Co., 1958. Price $15.00.

A complete monograph on the subject, with emphasis on the experience and practice at the Massachusetts General Hospital. Most of the color plates are borrowed from Fletcher Woodward and others.

Fortschritte der Kiefer- und Gesichts-Chirurgie. (Advances in Maxillofacial Surgery)

Volume IV of a Yearbook issued by *Prof. Dr. Karl Schuchardt*, Direktor der Klinik und Poliklinik für Zahn, Mund und Kieferkrankheiten der Universität Hamburg, with many contributions by German and foreign authorities. 4to, cloth, viii - 441 pp., 314 illustrations, 20 tables. Stuttgart, Georg Thieme Verlag, 1958. (Intercontinental Medical Book Corp., N. Y.). Price $28.55. In German.

Histopathologie der Tumoren der Kiefer und der Mundhöhle. (Histopathology of Tumors of the Maxilla and the Oral Cavity)

By *Prof. Dr. Med. Erich Langer*, Oberarzt am Pathologischen Institut der Medizinischen Akademie in Düsseldorf. Cloth, 4to, viii - 167 pp., 212 illustrations. Stuttgart, George Thieme Verlag, 1958. (Intercontinental M. B. C.). Price $11.80. In German.

Hormone Production in Endocrine Tumours

By numerous authors at a Ciba Foundation Colloquium on Endocrinology. Edited by *G.E.W. Wostenholme, O.B.E., M.A., M.B., B.Ch.*, and *Maeve O'Connor, B.A.* Cloth, 8vo, xii - 295 pp., illustrated, with a Cumulative Index to Vols. 1 to 12. Little, Brown & Co., 1958. Price $9.00.

Neurological Basis of Behaviour

By numerous authors participating in a Ciba Foundation Symposium. Edited by *G.E.W. Wostenholme, O.B.E.*, and *Cecilia M. O'Connor, B.Sc.* Cloth, 8vo, x - 400 pp., illustrated. Boston, Little, Brown & Co., 1958. Price $9.00.

Nursing in Diseases of the Eye, Ear, Nose and Throat

From the Manhattan Eye, Ear and Throat Hospital, with the following contributors: *Richard J. Bellucci, M.D., Richard E. Beulieu, M.D., Hazel Emmett, R.N., Eleanor E. Faye, M.D., R. Townley Paton, M.D., William F. Rabbett, M.D., Elizabeth K. Sullivan, M.A., R.N., F. H. Theodore, M.D.* Cloth, xv - 269 pp., 83 illustrations, 10th edition. W. B. Saunders Company, Philadelphia, Pa., 1958. Price $4.50.

Le Reflux Gastro-Oesophagien. (Gastroesophageal Reflux)

By *MM. P. Blondet*, Ex. Chef de Clinique Medicale á la Faculté, *J. Gaillard*, Oto-rhinolaryngologiste des Hopiteaux, et *P. Michaud*, Professeur Agrégé a la Faculté Chirurgien des Hopiteaux. Paper, 4to, 158 pp., illustrated. Paris, Expansion Scientifique Francaise, 1958. Price fr 2600. In French.

"The term Gastroesophageal Reflux is limited to the involuntary passage into the esophagus of part of the stomach contents without nausea, efforts at vomiting or the participation of the gastric musculature."

A comprehensive monograph.

The Thorax

By *David L. Bassett, M.D.*, Professor of Anatomy, Stanford University.

Section IV of the Stereoscopic Atlas of Human Anatomy is in two volumes and contains 140 pairs of exceptionally fine stereo films in color, mounted on twenty Viewmaster reels. Each view is complemented by a full-page, scaled line drawing which permits detailed labeling.

The photography, as before, is by Mr. William B. Gruber, and the line drawings are by Mrs. Lorene Sigal, whose fine work graced the two previous sections. A complete index is included.

Published by Sawyer's, Inc., Portland, Oregon.

Tumori Orbito-paranasali. Studio Clinico

By *Riccardo Fregni* and *Attilio de Poli* of the Otorhinolaryngological and Ophthalmological Clinics of the University of Milan. Large 8vo, paper, 333 pp. Complete monograph. Suppl. xxxiii (1957) of the Archivio Italiano di O. R. L.

Water and Electrolyte Metabolism in Relation to Age and Sex

A collection of eighteen papers delivered at a Ciba Foundation Colloquium, edited by *G.E.W. Wostenholme, O.B.E.*, and *Cecilia M. O'Connor, B.Sc.* Cloth, 8vo, 328 pp., illustrated. Boston, Little, Brown & Co., 1958. Price $8.50.

Of special interest to Otolaryngologists.

Notices

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY HOME STUDY COURSES

The 1958-1959 Home Study Courses in the basic sciences related to ophthalmology and otolaryngology, offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, will begin on September 1 and continue for a period of ten months. Detailed information and application forms may be secured from Dr. William L. Benedict, the executive secretary-treasurer of the Academy, 15 Second Street, S.W., Rochester, Minnesota. Registrations should be completed before August 15.

TEMPLE UNIVERSITY SCHOOL OF MEDICINE AND HOSPITAL

Postgraduate Course in Broncho-Esophagology February 16th to 27th, 1959.

Postgraduate course in Laryngology and Laryngeal Surgery April 13th to 24th, 1959.

These courses are to be given in the Department of Laryngology and Broncho-Esophagology, Temple University Medical Center, under the direction of Drs. Chevalier L. Jackson and Charles M. Norris.

The tuition fee for each course is $250.00. Application blanks and further information concerning dates of subsequent courses may be obtained by writing to: Jackson-Research, Lab 604, Temple University Medical School, 3400 N. Broad Street, Philadelphia 40, Pa.

TEMPLE UNIVERSITY

There will be a postgraduate course in Bronchoesophagology November 3 to 14, 1958, and a postgraduate course in Laryngology and Laryngeal Surgery December 1 to 12, 1958, given in the Department of Laryngology and Bronchoesophagology, under the direction of Drs. Chevalier L. Jackson and Charles M. Norris.

The tuition fee for each course is $250. Further information can be obtained from Dr. Chevalier L. Jackson, 3401 N. Broad Street, Philadelphia 40, Penna.

AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION

The American Association for Cleft Palate Rehabilitation will hold its 17th Annual Convention at the Sheraton Hotel in Philadelphia on Thursday, Friday and Saturday, April 30, May 1 and 2, 1959.

This Association is composed of medical, dental and paramedical specialists interested in the subject.

COLLOQUE INTERNATIONAL SUR COMMUNICATIONS ET LANGAGES

This conference, organized by the Faculty of Medicine of the University of Paris, under the auspices of the Department of Otorhinolaryngology of the Société Francaise de Phoniatrie, and the Laboratory of Acoustic Physiology of the Section of Neurophysiology of the Collège de France, will take place in Paris at the Faculté de Médecine, 45 rue des Saints Pères, Paris 6e, January 22-25, 1959.

The subject of language and communication in general will be discussed under its philosophical, physical, physiological, pathological, psychological and statistical aspects.

Professeur Aubry will preside. The Secretary-General is Doctor Vallancien, 16 rue Spontini, Paris 16e.

AERO MEDICAL ASSOCIATION

The 30th Annual Meeting of the Aero Medical Association will be held at the Statler Hotel, Los Angeles, California, April 27-29, 1959. Charles I. Barron, M.D., Lockheed Aircraft Corporation, will be the General Chairman.

AMERICAN LARYNGOLOGICAL ASSOCIATION

Copies of the Transactions of the American Laryngological Association are available for general distribution at $8.00 a copy. Please send request with check to Dr. James H. Maxwell, Editor, Transactions, Out-Patient Bldg., University Hospital, Ann Arbor, Mich.

ANNALS

The ANNALS wishes to repurchase copies of the March 1955 and the March 1957 issues, which are out of print, at two dollars a copy. These should be delivered to Manager of the ANNALS, P. O. Box 1345, Central Station, St. Louis 88, Mo.

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President: Francis W. Davison, M.D., Danville, Pennsylvania
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American Laryngological Association

President: Fred W. Dixon, M.D., Cleveland, Ohio
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Chairman: Victor R. Alfaro, M.D., Washington, D.C.
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Meeting: Atlantic City, June 8-12, 1959

American Otological Society

President: Moses M. Lurie, M.D., Boston, Mass.

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Meeting: The Homestead, Hot Springs, Va., March 13 and 14, 1959

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President: Joseph W. Hampsey, M.D., Grant Bldg., Pittsburgh 19, Pa.

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The Society of Military Otolaryngologists

President: Lt. Colonel Stanley H. Bear, USAF (MC)

Secretary-Treasurer: Captain Maurice Schiff, MC, USN, U. S. Naval Hospital, Oakland, California

Canadian Otolaryngological Society

President: Dr. G. Arnold Henry, 170 St. George St., Toronto, Ontario

Secretary: Dr. Donald M. MacRae, 324 Spring Garden Road, Halifax, Nova Scotia

Meeting: Sheraton-Brock Hotel, Niagara Falls, Ontario, October 9 and 10, 1959

Mexican Society of Otolaryngology

President: Dr. Rafael Giorgana

Secretary: Dr. Carlos Valenzuela, Monterrey 47 Mexico 7, D.F.

Pan-American Association of Oto-Rhino-Laryngology and Broncho-Esophagology

President: Dr. Jose Gros, Havana

Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40, Pa.

International Bronchoesophagological Society

President: Dr. Jo Ono, Tokyo

Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40, Pa.

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